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ROENTGENOLOGIC STUDY OF INTRATHORACIC LYMPHOBLASTOMA

By B. R. KIRKLIN, M.D. *and* HANS W. HEFKE, M.D.*

Section on Roentgenology, The Mayo Clinic

ROCHESTER, MINNESOTA MILWAUKEE, WISCONSIN

THE group of diseases which attack primarily the lymphatic system is often designated by the generic term lymphoblastoma, or malignant lymphoma. It comprises mainly the lymphosarcomas and lymphogranulomatous conditions (Hodgkin's disease), but includes also the various types of leukemia. When Hodgkin, in 1832, described the disease to which his name is given, he probably included cases of the entire group. Virchow, in 1842, separated from the entire group the various forms of leukemia and in 1864 the lymphosarcomas. Paltauf and Sternberg, in 1896 and 1898, separated lymphogranulomatosis from the group and considered this disease to be a chronic inflammatory rather than a blastomatous process. The term Hodgkin's disease has since been applied only to this entity and not to the whole group of lymphoblastomas. It is often impossible, even from a pathologic-anatomic standpoint, to distinguish Hodgkin's disease from lymphosarcoma, or lymphosarcoma from leukemia. In fact, many cases have been described in which pathologic evidence of two, or of all three, of these diseases was found in the same case. At all events it is often impossible to make the clinical differential diagnosis. The treatment is along the same lines, and the prognosis is practically the same.

The etiology of any of the group is not clear. It is commonly held that the disease which is called lymphogranulomatosis, or Hodgkin's disease, is a chronic inflammatory process. Fraenkel and Much have stated that they consider it a chronic form of tuberculosis of the lymphatic system, because they were able to demonstrate, in a high percentage of their cases, a granular form of *Mycobacterium tuberculosis*, and succeeded in producing tuberculosis in animals by inoculating them with material from lymphogranulomatous nodes. Their viewpoint, however, is not generally accepted, and other bacteria have been described as causative factors. At the present time there is no definite knowledge as to this detail. Certain pathologists consider the manifestation of the disease to be a blastomatous process, largely because it sometimes exhibits infiltrating growth. In the opinion of some investigators the different types of leukemia may be caused by a chronic infectious process. Others consider the neoplasms seen in leukemia to be malignant growths of the leukopoietic system. Lymphosarcoma, as the name implies, is supposed to be a sarcoma originating from lymphatic cells.

Webster has written that he considers it probable that lymphosarcoma and lymphatic leukemia are different manifesta-

* Former fellow in Radiology, The Mayo Foundation, Rochester, Minnesota.

tions of the same disease. According to Sternberg, the position of lymphosarcoma among the diseases of the lymphatic tissue is not clear. Fraenkel, Schmidt and Pappenheim have expressed their views that there is a close relationship between lymphosarcoma and the various forms of pseudoleukemia or of lymphadenosis. The latter term belongs to all diseases in which there is marked increase in myeloid or lymphatic tissue, either with increase of the number of leukocytes in the blood (leukemia) or without increase (aleukemia). It seems, therefore, that most authors regard Hodgkin's disease as a definite clinical and pathologic entity, whereas lymphosarcoma, leukemia and aleukemia are generally considered to belong to one group, styled lymphadenosis by Sternberg.

Our study pertains primarily to roentgenologic manifestations in the mediastinum and the lungs. The series comprises 67 cases, including 40 cases of Hodgkin's disease, 17 of lymphosarcoma and 10 of leukemia. All these cases were seen in The Mayo Clinic within the period 1927 to 1930 inclusive. In order to study the three diseases separately, only those cases were included in which pathologic-anatomic diagnosis was made, either by biopsy or necropsy. In many cases which were not taken into consideration in our study, clinical examination and response to roentgen therapy proved that they belonged to the general group of lymphoblastoma, but further separation into the three types of disease was not possible.

Among the 40 patients who had Hodgkin's disease, 26 were males and 14 were females. Pathologists with special experience in this field, such as Fraenkel, MacCallum and Kaufmann, and certain clinicians, among them Ziegler, Kruchen, and Lemon, have noted that males are much more susceptible to Hodgkin's disease than females. Ziegler, in reviewing the literature, found that the proportion of women is only 35 per cent; Kruchen, in his review in 1928, found a ratio of 32 per cent. Only Sternberg had the impression that there was little difference in distribution by sexes. The age stated in most reviews is between twenty and forty years. Lemon gave the average age of men suffering from Hodgkin's disease as thirty-five and of women as thirty-four years. Reed alone considered young persons to be attacked oftener than those of middle age. The average age of our patients who had Hodgkin's disease is thirty-two years; 75 per cent of all patients were between the ages of twenty and forty years; the oldest patient was fifty-five, and the youngest, seven years.

In the group of patients who had lymphosarcoma, the average age was thirt eight years; the oldest patient was aged fifty-five and the youngest six years. There were 10 males and 7 females. In a small group of patients with leukemia, the average age was thirty-seven years; the oldest was aged forty-eight years and the youngest, eight years. Six were males and 4 females.

We have tried to find out also in what proportion of all cases of the conditions under consideration a lesion was roentgenologically demonstrable, either in the mediastinum, in the lungs or in both. Most writers state only that the mediastinum is very often involved. Wessler and Greene found mediastinal involvement in 100 per cent of their cases of Hodgkin's disease. Whitaker reported mediastinal involvement, proved by necropsy in 7 of 22 cases (about 30 per cent) and Kruchen in about 65 per cent.

We found that evidence of thoracic involvement had been discovered in routine roentgenologic examination in about 49 per cent of the cases in which the diagnosis was Hodgkin's disease of any part of the body and in which this diagnosis had been proved by biopsy or necropsy.

Among cases of lymphosarcoma evidence of pulmonary or mediastinal involvement was found in only about 20 per cent or in 17 cases of a total of 84 in which a diagnosis had been made by biopsy, or in which specimens were obtained during operation.

Many of these lymphosarcomas were confined to the abdominal cavity; apparently they primarily involved the lymphatic system of the stomach or intestines.

Among 48 cases of leukemia, with typical blood picture, involvement of the thorax was found in 10 cases. Of these cases, 6 were instances of chronic lymphatic leukemia, two of chronic myelogenous leukemia, and two of acute leukemia. We have not been able to find any definite statements concerning the frequency of involvement of the thorax or mediastinum in leukemia, although such involvement has been described. Von Domarus, in a review of the literature, noted that mediastinal tumors are rarely or never found in myelogenous leukemia, but that the various forms of lymphatic leukemia and of lymphadenosis lead to involvement of the mediastinum and hilar nodes rather often.

Soon after the discovery of roentgen rays, they were used to demonstrate the presence of mediastinal tumors and enlarged mediastinal and hilar nodes. Clinicians and roentgenologists frequently have written on the subject. We shall mention only the more important articles. Ziegler, in 1927, and Kruchen, in 1929, gave an extensive bibliography.

Wessler and Greene, in 1920, reported 25 cases of lymphogranuloma with positive thoracic manifestations. They wrote that they considered it possible to make a roentgenologic diagnosis of Hodgkin's disease in a considerable number of cases, and to classify intrathoracic manifestations in four groups: (1) mediastinal tumors, expanding only; (2) an infiltrative type, with evidence either of invasion of pulmonary tissue from the nodes, or of diffuse transformation of intrapulmonary lymphatic tissue into granulomatous tissue; (3) isolated nodules, producing circular or oval shadows of moderate density in the lung, and representing isolated foci originating in preëxisting lymph nodes, and (4) discrete nodes at the hilum, extending for a considerable distance into the lung, and of rather faint density. The most common manifestation which they found was that of group 4, and the most common feature of that group was a separate, distinct shadow in the right side of the mediastinum representing a diseased paratracheal node. Next in order of frequency followed groups 1, 2 and 3.

Lemon and Doyle reported clinical observations in 26 cases of Hodgkin's disease in 1921, and wrote that they considered the roentgenogram a very helpful and necessary diagnostic means, but did not expect an exact pathologic diagnosis from it. In general, they noted that Hodgkin's disease should be considered when the roentgenogram reveals a bilateral, feathery shadow extending from each hilum, and when there is bilateral mediastinal widening. In all but two of their cases, roentgenologic examination gave positive results.

Walton wrote that lymphosarcomas do not invade the tissue, but that they often displace the mediastinum and its contents; the Hodgkin's type might infiltrate the lungs, giving the impression of a tuberculous lesion; the enlarged nodes are usually oval, either single or massed together. According to Kahn, Hodgkin's disease and lymphosarcoma cannot be distinguished from each other roentgenologically. Chaoul and Lange mentioned the difficulties in diagnosing pathologic entities when a mediastinal tumor can be demonstrated. They have seen infiltration of the lungs from nodes fairly often in lymphogranuloma; the appearance might resemble that of a primary carcinoma of the lung or bronchus.

Weiss, in 1923, wrote that he considered it sometimes impossible to make a diagnosis of Hodgkin's disease roentgenologically, because primary and secondary malignant tumors and benign tumors must be distinguished from it. According to Childs, the usual picture in Hodgkin's disease is a dense, bilateral, paratracheal shadow which is either irregular in outline, or circumscribed and well defined; only occasionally a unilateral mass projects at the level of the hilum.

The most comprehensive data on the

roentgenologic manifestations of Hodgkin's disease were published in 1923 by Whitaker. He reported 40 cases and considered the roentgenographic appearance of this disease sufficiently characteristic to be of great value in the differentiation from other forms of malignancy and from tuberculosis. For the classification of the different types, the four groups of Wessler and Greene were used. Among Whitaker's 40 cases, there were discrete nodules in the hilar region in 33, which is a characteristic of group 4; in 22 there was evidence of a mediastinal tumor, a characteristic of group 1; in 11 pulmonary infiltration was evident, a characteristic of group 2; characteristics of group 3 were not found in any case. Whitaker expressed the opinion that lymphosarcoma cannot be distinguished from lymphogranulomatosis, by the roentgenogram. Sometimes, according to him, Hodgkin's disease might simulate sarcomatous or carcinomatous metastasis, but metastatic nodules are usually somewhat more dense and discrete. Isolated shadows in the lungs are considered by him to be evidence against Hodgkin's disease, although few such cases have been described. Whitaker wrote that he considered tuberculosis to be the most difficult disease to rule out roentgenologically.

Melville has expressed himself as regarding fairly well defined mediastinal tumor as the typical roentgenologic picture of Hodgkin's disease, but he admitted that some other mediastinal growths might simulate it. Often, also, he said a differential diagnosis from aneurysm, sarcoma, and substernal goiter must be made. Holland, in discussing Melville's paper, said that he did not expect too much from the roentgenologist in the diagnosis of mediastinal tumors.

Dietlen, in 1927, stated that it is easy to find mediastinal changes roentgenologically but that differentiation into the different pathologic classes might be very difficult; aneurysms, lymphosarcomas, substernal goiters, Pott's abscess, mediastinitis, and dilatation of the esophagus might produce similar pictures. Hodgkin's disease, he continued, seems to attack the paratracheal lymph nodes first, not the hilar nodes. He said that it can be distinguished from lymphosarcoma by the fact that the lesions appear to be lobulated and do not often displace other organs; lymphogranuloma (Hodgkin's disease) infiltrates the tissue of the lung fairly often. Such changes in the lung itself, he stated, are not as rare as is usually maintained; they might simulate bronchopneumonic regions, or lesions of tuberculosis, or they might resemble metastatic growths. Differentiation from leukemic mediastinal and pulmonary involvement seemed impossible to Dietlen.

Ziegler also emphasized the fact that pulmonary involvement is more common than is usually believed. The process, he stated, may spread from the bronchial nodes, and a few smaller or larger nodules may be found in the pulmonary tissue, or large parts of a lobe may be infiltrated. Definite, but irregular, intense mediastinal shadows, with or without pulmonary involvement, he said, were characteristic.

Blum, in 1928, reported a case of Hodgkin's disease without mediastinal involvement, but with evidence of a definite, isolated nodule in the lung. This was verified at necropsy. A roentgenologic differential diagnosis was not possible. After roentgen therapy, according to Presser, the lobulated contour of the mediastinal masses in Hodgkin's disease and lymphosarcoma is replaced by a more linear and narrower shadow. This occurred in all his cases. Renewed activity in the nodes was exhibited in widening and lobulation of the shadow. Belden, in 1928, considered the "baffling and unsatisfactory" roentgenographic diagnosis of mediastinal diseases. He expressed his thought as follows: mediastinal tumors only rarely involve the lung; their bilateral distribution distinguishes them from pulmonary bronchial carcinoma; a lobulated border is the most common feature of Hodgkin's disease, together with a well defined outline; evidence of Hodgkin's disease might also be circumscribed, isolated

foci in the lung, or a large mediastinal tumor, without evidence of individual nodes, and with or without invasion of the lung.

Kruchen, in 1929, stated that the best known picture of Hodgkin's disease is that of a nodular, bilateral mediastinal tumor. Less often seen and more difficult to diagnose, he stated, are isolated round tumors representing hilar or bronchial nodes; moreover, atelectasis and compression of the lung, vessels, or trachea are rarely seen.

It is difficult to find precise statements as to the diagnostic points in lymphosarcoma of the mediastinum and lungs. Apparently many authors do not distinguish between Hodgkin's disease and lymphosarcoma. Some consider a mediastinal tumor without lobulation as typical of lymphosarcoma. Evidence of separate nodes is considered by them as being against the diagnosis of sarcoma. However, no special article dealing with the roentgenologic diagnosis of lymphosarcoma in the thorax could be found. The same holds true of leukemia. Only occasional mention is made of roentgenologic signs in the mediastinum and lungs. Otten described nodes involved by leukemia as well defined and situated in the mediastinum or hilum, and without infiltrative tendencies. Von Domarus said that enlargement of the hilar nodes in lymphatic leukemia is often not demonstrable; a mediastinal tumor might easily be confounded with other mediastinal growths. Infiltration into the lung, according to him, happens only rarely. Joachim and Loewe described a case in which definite involvement of the lung was complicated by repeated infarcts which made the roentgenologic diagnosis difficult.

In studying the roentgenologic signs of Hodgkin's disease we have endeavored to classify our cases in two main groups. The first group comprises the cases in which the nodes only were attacked, either the nodes of the mediastinum only, or the more or less separated hilar nodes, or both. In the second group are the cases with involvement of the pulmonary tissue, either infiltrative or metastatic, with or without nodal mediastinal involvement. From a pathologic standpoint, this classification seems more serviceable than the four groups of Wessler and Greene, and simpler

Fig. 1. Hodgkin's disease with multiple discrete nodes in both hila.

and more practicable for differential diagnosis. Of our 40 cases, 62.5 per cent belonged to group 1; that is, 25 of them presented involvement of the nodes of the mediastinum and hilum, and the lungs were free of disease. In 5 cases, definitely localized, discrete nodes were demonstrable in one hilum or in both. In the 40 cases, localized nodes were present on one or both sides in 32.5 per cent, or 13 cases. In 2 cases in which there was no mediastinal widening, there was distinct enlargement of the hilar nodes. Only one case could be found in which neither mediastinum nor hilum was the seat of the disease, although there was definite involvement of the lung. The localized, separate nodes produced well-defined, regular, round or oval shadows (Fig. 1). Their density was somewhat less than that of the mediastinal mass, apparently on account of their comparatively smaller

Fig. 2. Hodgkin's disease with extensive involvement of the right hilum.

size. A definite, fairly well distinguishable shadow of a paratracheal node on the right side, considered to be of great diagnostic importance by Wessler and Greene and Whitaker, was seen in 26 cases. The widened mediastinal shadow was most often lobulated, corresponding to the make-up of the mass by several separate enlarged nodes. Often the lobulation was very marked, but sometimes it was slight. The density of the shadow was usually about the same as that of the normal mediastinum; however, the edges, especially the lobulated margins, usually were somewhat less dense. In 8 of the 40 cases the involvement was unilateral: in 7 cases the right side was affected (Fig. 2), whereas in only one case the disease was limited to the left side. The observation of Presser regarding the change of contour of the mediastinal tumor, from a lobulated to a straight line, by roentgen therapy, was confirmed in 14 of the 18 cases in which treatment was given at the Clinic, and in which reëxamination was carried out afterward. The value of the reappearance of lobulation as a sign of recurrence could not be followed up, for many patients arrange for their roentgen therapy with roentgenologists who are closer to their homes. Straightening of the contour, of course, accompanies narrowing of the tumor. We found, as other observers found, that displacement of surrounding structures, especially the trachea, is exceedingly rare even when mediastinal masses are tremendous. In only one of the 37 cases in which there was mediastinal involvement, was the trachea displaced. In this case the mass was large, unilateral, and obscured the upper portion of the right lung. In other cases in which by far the greatest expansion of the tumor was on one side, no apparent deviation of the trachea could be shown. That fluid in the pleural spaces secondary to Hodgkin's disease, or fibrosis of the lungs, may cause displacement, is obvious, and occurred in one of our cases after radium therapy.

Invasion of the lungs was seen in 12 cases (30 per cent). It has been mentioned previously that in only one of these cases were enlarged nodes in the mediastinum or hi-

Fig. 3. Extensive infiltration in Hodgkin's disease resembling pulmonary malignancy.

lum lacking. In 2 of these cases there were enlarged hilar nodes in combination with pulmonary involvement; in the other 9 there was definite mediastinal widening. Infiltration into the lungs, originating from the affected nodes, was most frequently encountered. A picture which is ordinarily typical of metastasis, and which is characterized by discrete, well defined, round or oval soft shadows in the pulmonary fields was found in only 5 cases. In one case, the appearance was that of a primary carcinoma of the lung which involved an entire upper lobe, but which cleared up after roentgen therapy (Figs. 3 and 4). The majority of the lesions gave the impression of having broken through the capsule of the node and of directly invading the lung, occasionally simulating a primary carcinoma of the bronchus. A few involved the lung in the form of patches that resembled the appearance in bronchopneumonia. The nodules, however, were much denser and not widely separated from each other. In 2 cases, the appearance presented was that of extensive bronchiectatic portions with

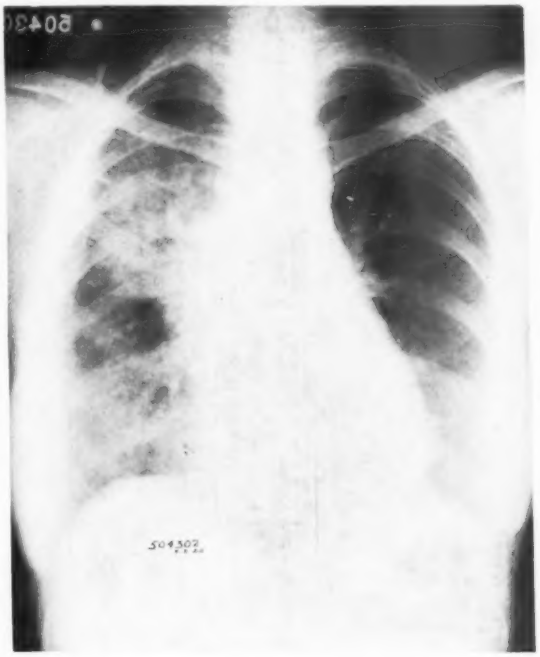

Fig. 4. Same case as shown in Figure 3 after roentgen treatment.

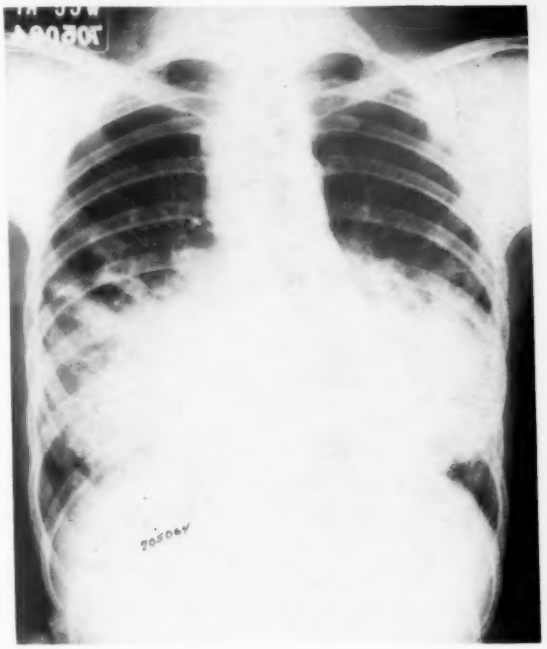

Fig. 5. Hodgkin's disease infiltrating both lungs. Also large nodes in the upper right side of the mediastinum.

marked surrounding inflammatory reaction (Fig. 5). Extensive involvement of the lung seemed to be a late complication, for it was confined to cases of well advanced disease and to patients who were in poor general condition. It was not possible to follow the effect of radiation in a sufficient number of cases to make certain that any definite changes had taken place in the roentgenologic picture. Small regions of pulmonary involvement were seen to disappear entirely afterward. Of special interest was the case in which the lung was affected by Hodgkin's disease, without any apparent affection of the mediastinal or hilar nodes (Fig. 6). It presented a fairly large, round, well circumscribed, soft shadow in the left side of the thorax, similar to the shadow in the case described by Blum. There are no characteristics which enable such a picture to be distinguished from that of a single carcinomatous or sarcomatous metastatic growth. A pleural plaque can easily be excluded by stereoroentgenograms of the thorax. The pres-

Fig. 6. Single isolated nodule resembling metastasis at the left border of the heart (Hodgkin's disease).

ence of fluid in the pleural cavity was detected in 3 cases (about 7.5 per cent). The diaphragm was elevated in 3 cases, possibly by pressure on the phrenic nerve by mediastinal masses, possibly by masses in the abdomen.

In this series the most common roentgenologic feature of Hodgkin's disease in the thorax was bilateral, lobulated widening of the mediastinum, with or without enlargement of the hilar nodes. Lobulated widening was usually present, also, when the lungs were involved.

The 17 cases in which lymphosarcoma was microscopically confirmed were grouped in the same manner. All of them exhibited nodal enlargement either in the mediastinum, or the hilum, or both. It was surprising to find shadows indicating bilateral mediastinal widening, with definitely lobulated edges, in 10 cases (Fig. 7), and in only 2 cases a unilateral, large oval mass, which in the literature is most often considered to be typical of lymphosarcoma of the mediastinum. Localized, discrete hilar nodes were visible in 4 cases (about 23 per cent). Involvement of the lung, regarded by many observers as incompatible with lymphosarcoma, was noted in 4 cases (about 23 per cent) (Fig. 8). Always combined with it, however, was involvement of mediastinal or hilar nodes, except in one case, in which after considerable treatment there was pulmonary involvement, without demonstrable nodal enlargement. These sarcomatous changes in the lung were of the infiltrative type in 2 cases, and originated in the nodes. The disease was unilateral in 5 cases (about 30 per cent). The trachea was definitely displaced by a large tumor in one case. In 5 cases fluid could be demonstrated in the pleural cavity, and the diaphragm was elevated in one case.

The phenomena in the 10 cases of leukemia with mediastinal or pulmonary involvement were little different. In all cases there were definitely enlarged mediastinal (Fig. 9) or hilar nodes; the nodes were discrete in 5 cases. The edge of the region of mediastinal widening was straight in some cases and lobulated in others. In 4 cases there was definite pulmonary involvement

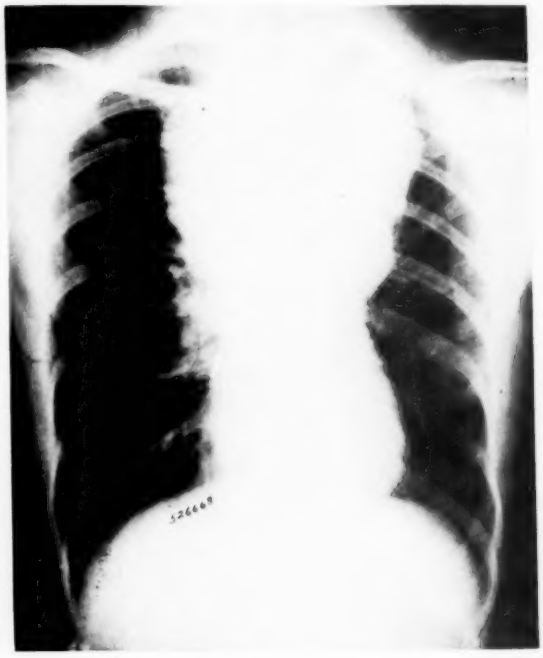

Fig. 7. Lymphosarcoma with bilateral mediastinal widening and lobulated edges.

of the infiltrative type. In one case the pulmonary involvement was in the form of a rather dense, large portion which had the appearance of an abscess. However, the clinical evidence and the disappearance of the lesion after irradiation proved it to be leukemic infiltration. In all cases the affected regions were bilateral. Fluid was not seen in any case. The diaphragm was definitely elevated in one case. Signs of compression or displacement of neighboring organs were not present.

On reviewing the roentgenologic data concerning the three diseases under consideration it would appear that there is no distinguishing roentgenologic sign of any of them. Any of the three may exactly resemble either of the other two, and, in view of their morbid anatomy, this might be expected. It is often impossible for the pathologist to make a gross diagnosis at necropsy, and he requires the microscope to make a precise diagnosis. The roentgenologist might sometimes be right if he considered bilateral involvement of the mediastinum, with multiple, discrete hilar nodes as being indicative of leukemia, or a large, unilateral tumor as being indicative of lymphosarcoma, but either manifestation occurs just as often in cases of Hodgkin's disease. All that should be expected of the roentgenologist is a broad diagnosis of lymphoblastoma, or of malignant lymphoma, if the latter term is preferred. Even this diagnosis often requires considerable study, and sources of error are numerous. The differential diagnosis must take into account aneurysm, benign tumors, substernal goiter, carcinomatous or sarcomatous metastasis, primary carcinoma of the lung or bronchus, tuberculosis of the lungs, Pott's abscess of the thoracic portion of the spinal column, marked dilatation of the esophagus, and mediastinitis. Roentgenoscopic examination of the thorax is usually indispensable to rule out aneurysm (pulsation, connection with aortic shadow, and so forth), and substernal goiter (tracheal tug). Tuberculosis is rarely confounded with malignant lymphoma. In only one case of our series was there difficulty, and in this instance calcification in the enlarged nodes, and lack of response to irradiation proved

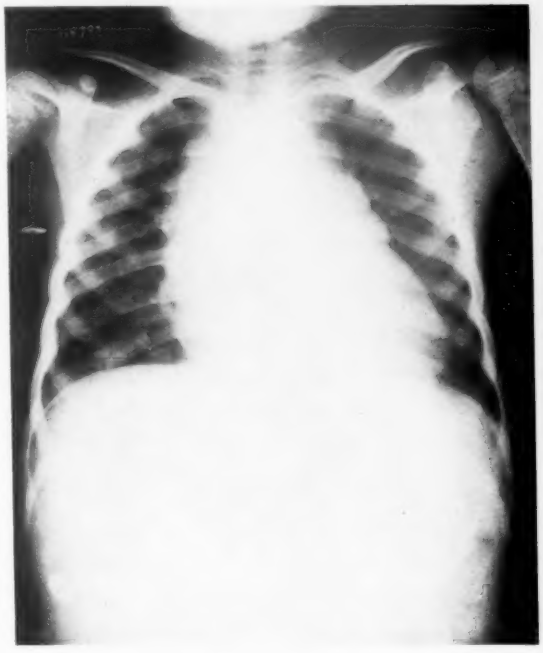

Fig. 9. Bilateral widening in a case of lymphatic leukemia.

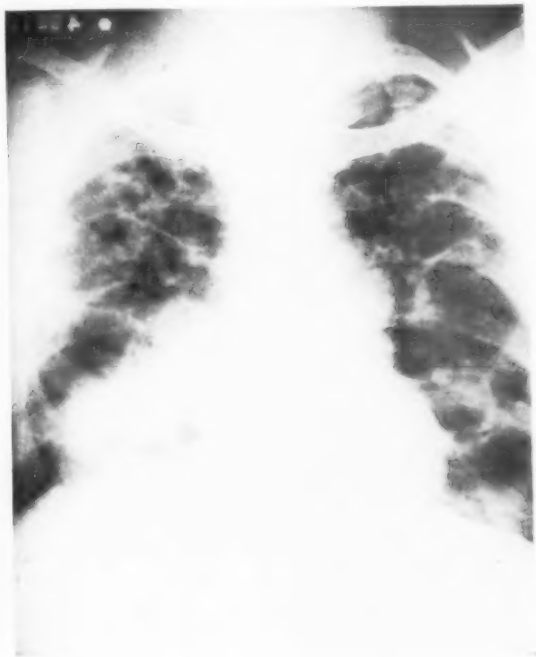

Fig. 8. Lymphosarcoma infiltrating the lung.

that the lesion did not belong in the group of lymphoblastomas. In a few cases a differential diagnosis cannot be made roentgenologically and one must be contented to describe the involvement of the mediastinum or lung, leaving exact diagnosis to correlation with clinical data. If this fails, a therapeutic test with roentgen rays will occasionally allow the diagnosis to be made. Usually the so-called lymphosarcomas diminish in size sooner and more rapidly than the lymphogranulomas, although this mark of distinction is not absolute.

SUMMARY AND CONCLUSIONS

1. Roentgenologic examination of the thorax in cases of Hodgkin's disease, lymphosarcoma, and leukemia does not permit a precise diagnosis of any one of these diseases. They must be considered as one group which might be called either lymphoblastoma or malignant lymphoma.

2. Demonstrable roentgenologic manifestations in the thorax may be expected in about 50 per cent of the cases of Hodgkin's disease, and in about 20 per cent of the cases of lymphosarcoma and of leukemia.

3. In the series reported, enlargement of the mediastinal and hilar nodes was the most common manifestation. Involvement of the lungs, either of the infiltrative or of the metastatic type, was found in 30 per cent of the cases of Hodgkin's disease, in about 23 per cent of the cases of lymphosarcoma and in 40 per cent of the cases of leukemia, whenever involvement of the thorax was demonstrable.

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ROENTGENOLOGIC STUDIES IN EARLY LOBAR PNEUMONIA*

By WALTER H. UDE, M.D.
Roentgenologist, Minneapolis General Hospital
MINNEAPOLIS, MINNESOTA

IT IS generally conceded that the demonstration of a triangular area of consolidation is frequently the earliest roentgenologic finding in lobar pneumonia. However, this has not been admitted to be the constant early finding in all cases. Thus Sante[6] distinctly recognizes "central" or "hilum" pneumonia which he conceives to be limited to the parahilar tissues and never to assume the cone-shaped distribution. He bases his opinion mainly on studies made from the usual posteroanterior or anteroposterior roentgenograms, and does not mention the use of lateral views to substantiate his opinion. Where the consolidation subsequently spreads to the lateral periphery, he thinks the early shadow indicates central origin of a true lobar pneumonia. Stephenson[7] also recognizes this medial density as indicative of hilum pneumonia. On the other hand, Weill and Mouriquand,[9] in a study of the roentgenologic findings in 350 cases, concluded that the early shadow is usually triangular, with its base always cortical. They have never seen a shadow which could be considered entirely central. Tripier,[8] in 1904, described the cone-shaped shadow, and stated that the consolidation

FIG. 1*a*. Anteroposterior roentgenogram, showing two triangular consolidations: one in the midportion of the left lung with the base of the triangle at the lateral periphery, the other in the right cardio-phrenic angle.

FIG. 1*b*. Same case as Figure 1*a*, right lateral film, showing rounded density overlying the hilum representing the left lateral triangle, and a posterior basal striated triangular density which represents the right-sided basal consolidation.

* From the Departments of Roentgenology of the Minneapolis General Hospital and the University of Minnesota, Minneapolis, Minnesota.

Fig. 1*c*. Left lateral view of a case having a similar left lateral triangular consolidation to that shown in Figure 1*a*. This shows a more sharply circumscribed density overlying the hilum, rounded anteriorly and flattened posteriorly where it is demarcated by the interlobar pleura.

always reaches the periphery. More recently Mason,[3] in a study of 37 cases of early lobar pneumonia in children, concludes that a central pneumonia in the strict sense never occurs.

The observations of Blake and Cecil[1] in their studies on experimental pneumonia in monkeys give us the best available pathologic description of the early pneumonic process. They conclude that "the pneumococcus primarily invades pulmonary tissue at some point or points in the portion of the lobe proximal to the hilum, that it spreads rapidly throughout the lobe by way of the perivascular, peribronchial and septal interstitial tissue and lymphatics, and that it quickly reaches the pleura." They likewise show that "the initial mode of invasion may be by direct penetration at one or more points into the walls of the larger bronchi near the hilum . . . . In harmony with the mode of distribution of pneumonia it has been found that the initial lesions of lobar pneumonia are of the interstitial framework of the lung. . . . Hepatization begins centrally and spreads toward the periphery and is a constantly progressive process." In their pathologic analysis of a very early consolidation they find the process entirely limited to the interstitial tissues, with the alveoli free from exudate, but somewhat atelectatic. This latter observation was recently referred to by Coryllos and Birnbaum as corroborating their studies on "pneumococcic lobar atelectasis."

The present study is based on 120 cases of lobar pneumonia, 50 of which were seen in the early stage of the disease, at which time they presented cone-shaped densities on roentgen films. The study limits itself to the roentgenologic findings in this stage of the disease, with emphasis on the correct interpretation of the process familiarly known as "central" or "hilum" pneumonia. These studies were made at the bedside,

Fig. 2*a*. Anteroposterior roentgenogram, showing minimal density in right cardio-phrenic angle, mainly retrocardiac.

Fig. 2*b*. Same case as Figure 2*a*, right lateral view. A posterior basal triangular density is demonstrated.

and include lateral as well as the usual anteroposterior examinations.

In all of these early cases of lobar pneumonia we were able to demonstrate that the consolidation assumed a conical distribution with the base of the cone toward the periphery, and that the periphery may be lateral, anterior, or posterior. The triangular shadows whose bases are directed laterally are best shown in the anteroposterior view, and appear as rounded densities in the lateral view. Figure 1*a* shows two pneumonic triangular densities: one in the mid-portion of the left lung and directed laterally, the other in the medial portion of the right base. Figure 1*b*, the right lateral view, shows the density of the left lateral triangle overlying the hilar region, with the right-sided basal triangle extending downward posteriorly. Figure 1*c* is the left lateral film of a similar left lateral triangle, and shows a sharper outline of the shadow overlying the hilum. Its location is therefore the posterior mid-portion of the left upper lobe. These rounded shadows correspond with the diameters of the bases of the cones, and may resemble those of infarcts as described by Rieder and Rosenthal.[4] The lateral views also demonstrate the posterior and anterior triangles. Posterior basal triangles lie medially on the anteroposterior view and are often overshadowed in this view by the heart and diaphragm. Figure 2*a* presents the anteroposterior view of a case in which there was clinical evidence of pneumonia. This film shows an increased density overlying the right side of the heart, not well demonstrated in the reproduction. The lateral view (Fig. 2*b*) shows this to be due to a posterobasal consolidation. Triangles extending anteriorly are usually limited to the middle lobe on the right due to the lobar divisions of the lungs. Posterior triangles practically always involve the upper portions of the lower lobes, and these are the shadows which in the anteroposterior view give a rounded density overlying the

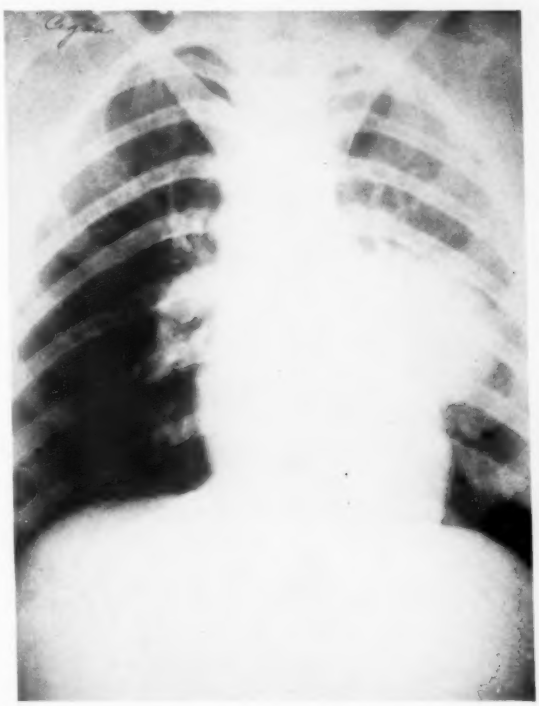

Fig. 3*a*. Anteroposterior view showing a rounded density overlying and extending from the left hilum, commonly interpreted as "central" or "hilum" pneumonia.

Fig. 3*b*. Same case as Figure 3*a*, left lateral view. The consolidation is triangular in shape, with its base in the posterior periphery, involving the upper part of the lower lobe.

hilum, and are therefore often interpreted as "hilum" or "central" pneumonia. Figure 3*a* shows such a rounded area of consolidation overlying and extending from the left hilum. The lateral view in Figure 3*b* shows the hilum and mediastinal clear space to be practically normal, with a density occupying the upper posterior portion of the lower lobe, the broadest diameter of the density being at the posterior periphery. The margins of the peripheral portion of this shadow demarcate the base of the cone which therefore shows as the rounded density in the anteroposterior view. Figures 4*a* and 4*b* show the two views of a similar case where the lateral film demonstrates a somewhat denser triangle with its apex definitely at the hilum, and its base in the posterior periphery.

We have studied 13 cases where the shadows in the anteroposterior view were of the "central" type, identical with Sante's illustration[6] of this type of pneumonia. In all of these cases the shadow was due to a posterior triangle, with the consolidation limited to the lower lobe. If these were true "central" pneumonias, one should find all of the lobes of the lung involved in their hilar portions. In 5 cases the process later showed extension into the lateral periphery of the involved lobe, while in the other 8 the consolidation remained limited to the medial portion of the lung. The latter cases therefore qualify entirely for the classification of "central" or "hilum" pneumonia. We therefore feel that we have sufficient evidence to conclude that the term "central" or "hilum" pneumonia is a misnomer, and that the term "early postero-medial" pneumonia would be more descriptive of this process.

An analysis of the triangular shadows indicates that the roentgenologic findings of early pneumonia in man can be correlated with the pathologic findings of Blake and Cecil.[1] The earliest roentgenologic findings are not those of a homogeneous triangle, but of a group of soft linear shadows ar-

Fig. 4*a*. Anteroposterior roentgenogram of a case similar to that shown in Figure 3*a*. The consolidation overlies the left hilum, and is partly overshadowed by the heart.

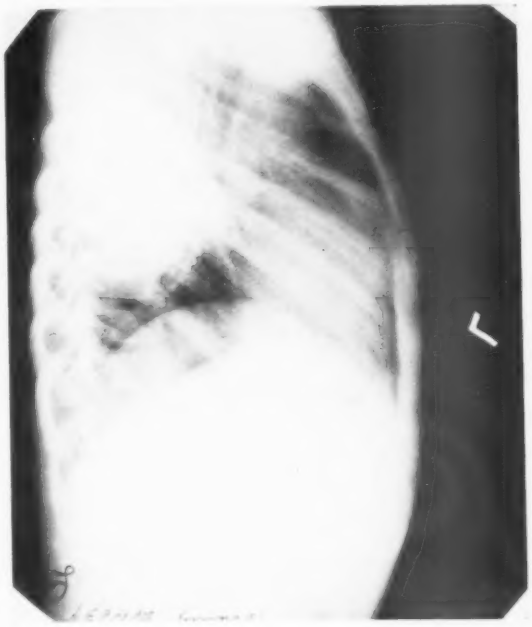

Fig. 4*b*. Same case as Figure 4*a*, left lateral view. The consolidation is shown to involve the upper part of the lower lobe, and to be triangular in shape, with the base of the triangle in the posterior periphery.

ranged in a triangular manner separated from each other by the air-containing bronchi. This may be interpreted as the stage of engorgement which, as Blake and Cecil demonstrated, is an interstitial process with very little alveolar involvement. It is only after the bronchi and alveoli are more or less filled with exudate that the shadow becomes homogeneous. The very earliest shadow consists only of this striated density, but the cases are usually examined too late to demonstrate it without also showing a more homogeneous density in the extreme periphery or base of the triangle. This latter density has been thought by some to point toward the peripheral origin of lobar pneumonia. Coryllos and Birnbaum claim that the more marked density at the periphery is due to atelectasis. This seems to be a plausible interpretation. The entire triangular density, however, can scarcely be due to atelectasis, as this is not confirmed by other investigators.

These roentgenologic studies were also correlated with clinical observations by Dr. George E. Fahr and his assistants of the medical staff of the Minneapolis General Hospital. A later publication by these investigators will report their studies.

SUMMARY AND CONCLUSIONS

1. The roentgenologic findings in early lobar pneumonia are analyzed and are correlated with the pathologic studies of Blake and Cecil.

2. Lateral as well as anteroposterior views, at the bedside, are advocated to demonstrate consolidations which may be overshadowed by the heart and diaphragm.

3. Lateral roentgenograms of so-called "hilum" or "central" pneumonia indicate that this term is a misnomer, that these medial shadows are in reality posterior cone-shaped consolidations, and that they may best be defined as "early posteromedial" consolidations.

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PEPTIC ULCER OF THE ESOPHAGUS

By J. RICHARDS AURELIUS, M.D.
SAINT PAUL, MINNESOTA

ALTHOUGH peptic ulcer of the esophagus was first described as long ago as 1839 by Albers, no real interest in the subject is noted until in 1906, when Tileston[6] carefully reviewed the 41 sporadic cases which had appeared in the literature during the interval and added 3 new cases that had come under his observation. His review and analysis brought the subject very completely up to date and clearly showed that peptic ulcer of the esophagus is a definite disease entity. Then interest in the subject lagged once more, and it was not until the report of 13 cases by Friedenwald, Feldman, and Zinn,[3] in 1928, that attention was again called to this subject.

Though the occurrence of peptic ulcer of the esophagus may be relatively infrequent, there seems no question, in view of the cases of healed ulcer seen at post-mortem examination, that it is not nearly as infrequent as we have thought it to be. It may be well to bear in mind the early history of duodenal ulcer, which shows how rarely this ulcer was recognized until it was looked for by the clinicians. Now, chiefly by virtue of the development of its roentgenologic picture, it has become a frequent finding.

Peptic ulcer of the esophagus heretofore has been found usually only at the post-mortem examination, but the fact that now comparatively many cases are described that have been diagnosed and proved clinically demonstrates that it does have a recognizable clinical picture, and this should be a stimulus for a more careful and insistent search for these lesions which are now going undiagnosed.

The roentgenologic literature is conspicuously lacking on this subject in spite of the fact that cases have been definitely recognized by roentgen examination. The roentgenological, as well as the rest of the clinical picture, is very incomplete as yet, and in the development of the diagnosis of this disease, the roentgenologist has a very important rôle to play. It is for this reason that the following single case is reported, hoping that even the report of single cases may help keep the subject enough in the foreground among roentgenologists so that in time there will be evolved means for a greater efficiency in the roentgen diagnosis of this condition.

The following case is reported in considerable detail in order not to overlook factors which, in the state of our present knowledge, may seem unimportant:

CASE REPORT

F. H., white, male, aged forty, weight 190 pounds, plasterer, was admitted to Ancker Hospital January 28, 1929, to the medical services of Drs. Goltz and Borg. The patient complained of pain in the epigastrium and of nausea and vomiting. He had been perfectly well up to the onset of the present illness three years before admission, when, for the first time, he noticed a slight burning sensation in the epigastrium. This was present about two years before he really paid much attention to it. It was most marked from one to one and a half hours after meals, and persisted until the next meal. During the last year this pain gradually became worse. He received relief from water, milk, or soda. The pain was felt in only one point which he designated as immediately under the xiphoid. It did not radiate, and never awakened him at night. He apparently had no definite remissions. His other chief complaint was nausea with vomiting at least once daily, which had been present for the six months preceding admission. This had become definitely worse in the last two weeks. Vomiting had no definite time relation to meals. Some relief was obtained from belching. He did not complain of dysphagia, had no hematemesis, no attacks of severe abdominal pain, no history of jaundice or melena. There was slight shortness of breath which he attributed to the epigastric pain. There were no other general or specific complaints. In the last few weeks the weight had dropped from 200 to 190 pounds. His past history was negative except for gonorrhea ten years previous to admis-

sion, measles and diphtheria in childhood, and influenza in 1918. The family history was negative. He smoked and used alcoholics moderately.

Physical examination revealed a well-nourished and very well-developed man having only a slight tenderness in the epigastrium. By systems the findings were negative. The blood examination on admission showed 82 per cent hemoglobin, 4,560,000 red blood cells, 8,150 white blood cells with 69 per cent polymorphonuclears, and 31 per cent lymphocytes. The blood Wassermann was negative. The urine showed a trace of albumin and occasional leucocytes. The electrocardiographic study was negative. The Ewald test meal showed fair digestion; 32.8 degrees of free HCl, 57.8 degrees total acids, and was positive for occult blood. The temperature course was normal throughout his stay in the hospital. On January 30, the oral Graham-Cole gall-bladder examination showed a normal response. The following day the roentgen examination of the gastrointestinal tract revealed a negative stomach and duodenum, and stereo views of the chest were also negative.

The patient then was put on ulcer diet regimen because of his suggestive history. He failed to get relief except symptomatically from the powders. On February 20, 1929, the Graham-Cole test was repeated and again showed a normal response. On February 28 the gastrointestinal examination was repeated and the stomach and duodenum were again found negative. However, during the roentgenoscopic examination there was seen a noticeable lag of barium in the lower end of the esophagus which was evidently due to a slight spasm, with a suggestion of a fleck of barium retention as seen in ulcer craters elsewhere. It corresponded exactly to the point of tenderness and pain of which the patient had consistently complained. Due to the patient's very large size and the impossibility of obtaining satisfactory plates, he was re-examined on the following day, when the same findings were present in the lower end of the esophagus at the cardia. The final roentgen report was: "Re-examination of stomach for comparison shows no retention and normal motility of the six hour motor meal. The stomach and duodenum are apparently negative. There is, however, an area in the lower end of the esophagus near the cardia which retains barium as do ulcers elsewhere in the gastrointestinal tract. This could be due to a lesion low in the esophagus. This corresponds definitely to the patient's complaint of soreness."

In view of these findings, Dr. D. G. Gardiner was asked to see the patient in consultation in regard to the advisability of esophagoscopy. Accordingly, on March 5, Dr. Gardiner made an examination of the esophagus and reported: "Esophagoscopy was unsatisfactory due to the size and lack of cooperation of the patient. Bleeding of the esophagus was noted as far down as view was permitted and at one place there was a little loss of substance of mucosa, but could not be sure that this was due to ulceration. Am satisfied that this bleeding was not due to trauma because esophagoscope did not go as far as origin of the bleeding."

On March 19, a second examination was made by Dr. Gardiner and the following report submitted by him: "Esophagoscopy shows a small ulcer near the cardia and overhanging the edge on the left posterolateral wall. The extent of the ulcer is not quite determined. The ulcer bleeds easily when touched. A specimen was taken from the edge of the lesion. "This biopsy specimen was examined by Dr. J. Noble, pathologist, who reported: "Specimen consists of biopsy of esophagus which is too small to describe grossly. Microscopically the section of the biopsy shows it to be covered by a layer of squamous epithelium. Beneath this there is a mass of glands cut on cross section. These resemble very closely glands of the stomach. One edge of the section resembles somewhat the picture seen in peptic ulcer. Between the glands there are numerous lymphocytes and at one point there is a suggestion of lymph nodes. Diagnosis: Peptic ulcer of the esophagus."

Therefore, with a clinical picture resembling peptic ulcer, with the lesion seen roentgenologically and confirmed by the direct observation of esophagoscopy and by the microscopic section from biopsy, a diagnosis of peptic ulcer of the lower end of the esophagus was made. Because dietary treatment had failed to give relief, the patient was transferred to the service of Dr. Gardiner, receiving treatment then by topical application of 5 per cent silver nitrate through the esophagoscope twice weekly for a period of eight weeks. The patient had immediate pain relief with the first treatment, and definite progressive clinical improvement associated with the disappearance of the ulcer by the end of the second month. A communication was received from the patient in April, 1930,

after one year had elapsed, in which he states that he feels entirely well, has none of his previous symptoms, has gained in weight and strength, and is working daily.

This case was interesting particularly because of the very suggestive history for

FIG. 1. Photomicrograph (low power). Squamous epithelium with glands beneath that resemble gastric glands in cross-section. Edge of section shows resemblance to gastric mucosa, with change as seen in erosion of peptic ulcer. See Figure 2 for this area with higher magnification.

ulcer of the stomach or duodenum, or possibly for cholecystitis, but with consistently negative roentgen findings for these conditions, and the lack of response to ulcer management. His complaint was unvarying

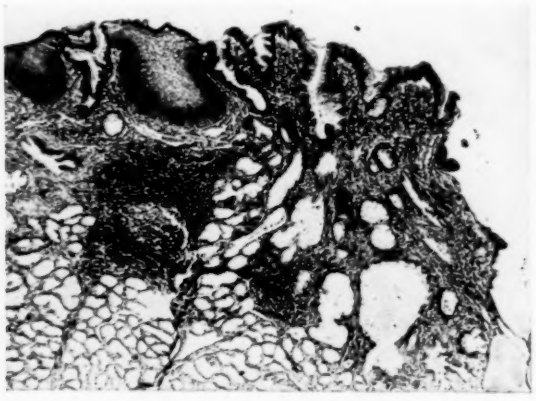

FIG. 2. Photomicrograph (high power). Showing transition from squamous epithelium to that resembling gastric mucosa with accumulation of lymphocytes in tissues beneath. The edge shows the erosion seen in the ulcer crater.

and apparently a true one. Being a very large man, he was hard to examine in every way, but that could not be considered a legitimate excuse for failure of diagnosis. Repeated examinations certainly were in order, and in this instance, their value was proved. Though his history was confusing and is still hard to explain in some of its phases, the fact that a lesion was found which, when properly treated, was cured promptly, only emphasizes our lack of information on this subject and shows the

FIG. 3. Roentgenogram of lower end of esophagus and of stomach, showing regurgitation of barium into esophagus with slight retention of barium in ulcer crater at point of arrow.

need for very close study to further develop its diagnostic criteria.

The literature on peptic ulcer of the esophagus is still relatively meager, but it is gradually bringing out a clinical disease entity with constant characteristics, and in the later writings we see less of the post-mortem reports and more of the reports of cases diagnosed in the living and successfully treated.

INCIDENCE

It is manifestly impossible to indicate what may be the actual incidence of peptic ulcer of the esophagus. The majority of cases that have appeared in the literature are from post-mortem examinations, many of which were accidental findings, or a few far-advanced cases that had been diagnosed clinically. That there are very many that heal spontaneously or because of therapy instituted for peptic ulcers supposedly in the stomach or duodenum must be acknowledged. With the continued refinement in diagnosis with the roentgen ray and the esophagoscope, we can expect a definite, increased recognition of this lesion.

The ulceration may appear at any age from infancy to senility, but it is most common in middle adult life. Tileston[6] found in his review that in 40 cases, 28 were in males and 12 in females. However, the 13 cases reported by Friedenwald, Feldman, and Zinn[3] show 6 were in men and 7 in women.

ETIOLOGY

The etiology of this ulceration is very likely on the same basis as that of peptic ulcers in the stomach and duodenum, and inquiry into it opens up the same controversies. Jackson[4] found in reviewing his cases of active peptic esophageal ulcers that more than 90 per cent had evidence of chronic foci of infection. He believes that the acute ulcer is perpetuated chiefly by the retrograde flow of gastric juice, and that the pain in these ulcers is due to these acid secretions, and not, at least to any appreciable degree, to the so-called cardiospasm, insufficiency of the cardia or of the diaphragmatic pinchcock. He also suggests that the presence of islands of gastric mucosa in the esophagus may be a factor in the etiology of peptic ulcer here, but not necessarily an essential one. Friedenwald, Feldman, and Zinn also agree that regurgitation of gastric secretions is an important etiologic factor, but they feel that it alone does not account for ulcerations due to the fact that ulcers do not form in all cases where regurgitation is not infrequent. Stewart and Hartfall[5] call attention also to the close association of these ulcerations to diseases where vomiting is a prominent symptom. They believe that in persons with considerable gastric heterotopia in the esophagus, there may be enough gastric juice formed to definitely delay the healing of an ulcer, especially if there is retention at the cardia of these acid secretions. The preponderance of ulcerations in the lower third of the esophagus over the other portions would seem to indicate more than a casual relationship between these acid secretions and ulceration.

PATHOLOGY

In 1906, Tileston[6] made the observation that the simple peptic esophageal ulcer resembled very closely the simple gastric ulcers. Later reports show that this opinion still generally prevails. The lesion may occur in any portion of the esophagus, but it is by far more common in the lower third. Some ulcers on the cardia edge are believed by Tileston to have their origin in the stomach and extend upward into the esophagus.

As elsewhere, the ulcer varies from very small to exceedingly large size. It may also vary from very superficial ulceration of the mucosa to penetration of all the layers with perforation into various structures of the chest. They have been described as elongated, oval, round, serrated or regular, single, multiple, or confluent, assuming apparently any of the forms that may be seen especially in duodenal ulcer. The appearance varies similarly depending on the acuteness or chronicity of the lesion. Tileston felt that these ulcers have a strong tendency to perforate, but this opinion was based on the cases he reviewed, most of which were seen at post-mortem examinations, and probably represented only a small part of the actual incidence of these ulcers clinically. The tendency to perforate, in view of all the recognized and assumed unrecognized ulcers of the esophagus, is

probably no greater than in other peptic ulcers. There is, however, a certain incidence of perforation with a very high mortality rate due to the fact that the perforation is likely to be followed by hemorrhage from the large vessels, mediastinitis, broncho-esophageal fistula with pulmonary complications, pericarditis, pleuritis, and empyema.

Microscopically the ulcer is similar to peptic ulcers of the stomach or duodenum. It heals by scar formation in degree according to the chronicity and size of the lesion. In the larger ulcers, a marked stenosis may result. Tileston reports a case by Ortman in which carcinoma was seen developing from the scar of an old peptic ulcer, and also one he himself had observed. Too few cases have been reported to accurately indicate a definite preference of site in regard to position on the anterior, posterior, or lateral walls.

The course seems characteristically to be that of a chronic lesion, with a slow, often insidious onset, being slowly progressive, with or without remissions, leading to healing by scar formation or death from perforation. It may have a duration of a few months to several years. Early recognition and effective treatment or spontaneous cure may lead to a definitely short course, but Jackson[4] has found that even with careful treatment locally through the esophagoscope and supported by general measures, some of these lesions may still be very slow to respond favorably.

SYMPTOMATOLOGY

Although pain and dysphagia are quite constant symptoms, it seems generally agreed that the lesion may be present for a long period of time before the patient becomes enough aware of the discomfort to seek relief. For this reason we can account to some degree for the discrepancy between the fairly frequent occurrence of scars as seen in post-mortem examinations and its recognition so rarely clinically.

Tileston has classified the most prominent symptoms as pain, dysphagia, vomiting, hemorrhage, and perforation.

The pain is a very constant symptom, felt usually under the lower end of the sternum or in the epigastrium when the lesion is low, and it may or may not radiate to the back between the scapulae. Its intensity varies widely though it is usually increased during deglutition and when this manifestation is present, it is strong evidence for ulceration in the esophagus in contrast to ulcers of the stomach and duodenum. Barclay[1] observed roentgenologically in an eighteen year old girl that the pain in swallowing was due to a rather marked spasm resulting when coarse food passed over the ulcer. Jackson,[4] however, attributes the pain chiefly to the acids present because of the prompt relief afforded by alkalies. Pain in his cases came on half an hour or longer after eating and sometimes continued throughout the night after the evening meal. This he attributed to regurgitation. He observed that only slight discomfort might be complained of by the passage of food, but sometimes a constant pain was induced by swallowing.

From these different observations by various writers, it is evident that pain is produced by irritating foods passing over the ulcer, by spasm, and by acids, and the character of the pain and the time of its occurrence will indicate which cause is active in producing the pain.

Dysphagia, also one of the cardinal symptoms, was present in all of the cases reported by Friedenwald, Feldman, and Zinn, and in 52 per cent of Tileston's cases. It varies in degree with the extent of the lesion and the type of food eaten, and is chiefly due to the spasm which occurs. This may become so marked that the patient eventually is unable to eat sufficiently to maintain normal weight, and in extreme cases may lead to marked cachexia. This symptom may appear only late in the disease, or, as in the case reported in this paper, it may never appear.

Vomiting was present in 71 per cent of Tileston's cases, being rare in some and

almost incessant in others. Often it was associated with other gastrointestinal lesions and sometimes it appeared to be reflex. Jackson found vomiting more commonly associated with ulcers near or in the hiatal constriction.

Hemorrhage was present in 23 per cent of the cases of Friedenwald, Feldman, and Zinn, and 53 per cent of Tileston's, the latter probably representing more chronic cases. The amount of blood may vary from slight streaking in regurgitated food, to profuse, rapidly fatal hemorrhages. The loss may be concealed as in other ulcer cases, and can be detected only as occult blood in the stools or in the vomitus, though the patient may be suffering primarily from the constant blood loss. A case of esophageal ulcer reported by Zahn in 1882 has evoked considerable interest with all reviewers of this subject because the patient had a red cell count of 950,000, and a diagnosis of pernicious anemia was made.

Perforation occurred in 14 per cent of Tileston's cases, but in none of those reported by Friedenwald, Feldman, and Zinn. This complication is generally fatal due to the structures accessible to these perforations.

DIAGNOSIS

Due to its usually insidious onset, its rather long course without definite symptoms, the inaccessbility of the esophagus for study before the development of the roentgenologic and direct methods of observation, there has been considerable difficulty in making a fairly early diagnosis of peptic ulcer of the esophagus. Its diagnosis until recently has rarely been made clinically until there occurred such late manifestations as perforation or stenosis. Tileston suggested that before an ulcer of the esophagus may be called peptic, we must rule out the other forms that may occur, namely the carcinomatous, decubitus, catarrhal, tuberculous, syphilitic, varicose, and those due to corrosive substances, foreign bodies, aneurysms, traction diverticula, thrush, and those occurring in the course of acute infections. Jackson has added also the rarely occurring blastomycosis and actinomycosis.

When such symptoms as substernal or high epigastric pain, a burning sensation under the sternum or dysphagia with regurgitation or vomiting, or with water-brash, or "heartburn" are present, a careful search for esophageal ulceration should be made. The roentgenologist has a real responsibility and opportunity here to make note of any suggestive findings and whether or not they can be definitely diagnosed as ulcers, they can be checked by esophagoscopy, and in the hands of a qualified esophagoscopist, their true nature can be determined. What may be only a suggestive finding by our present methods of study of the esophagus by the roentgen ray, may then become a lead to a positive clinical diagnosis by at least showing the indication for esophagoscopy.

Friedenwald, Feldman, and Zinn demonstrate definitely that these lesions can be diagnosed or at least strongly suspected roentgenologically, as shown by their group of 13 cases diagnosed clinically. They advise observing the esophagus under the roentgenoscope in different views, using, as a rule, a liquid barium mixture. They describe four types of defects that may be observed roentgenologically in the esophagus: (1) mucosal erosion, (2) niche, (3) spastic defects and (4) perforation.

The mucosal ulcer is the most difficult to demonstrate by the roentgen examination and is the one in which esophagoscopy is particularly valuable to check the slight findings. However, a small retention of barium in the crater may be present and it gives the characteristic fleck seen in peptic ulcers in the stomach and duodenum, and though this may be an inconclusive finding on the first examination, due to the tendency for small amounts of barium to remain fairly constant in the folds of the mucous membrane during the examination, a re-examination the next day may show the same findings and allow a positive diagnosis to be made. These small ulcers

may have varying degrees of associated spasm in the lower end of the esophagus which contributes materially toward making a diagnosis.

Friedenwald, Feldman, and Zinn have found the niche or penetrating type of ulcer the most frequent roentgen finding, and it corresponds to that of the gastric ulcer. These often show a barium fleck, and often the patient complains of pain as the barium passes over the ulcer. They consider the niche pathognomonic of ulcer of the esophagus.

The spastic defects they divide into three groups: (1) simple transient spastic defects causing retardation of the opaque meal, (2) a tapering defect of the esophagus towards the cardia and (3) an indentation resembling an incisura as seen opposite gastric ulcers.

The perforating ulcer is really a complication, and is rarely observed by the roentgen examination because the patient is too extremely ill to be examined. Strictures due to ulcers give the usual signs seen in other types which may vary from a slight lag of the barium to complete obstruction. They use both the roentgenoscope and plates to demonstrate the lesion, though the diagnosis is usually made by the former. At times they could demonstrate the lesion only by having the patient in the recumbent position and drinking the barium mixture through a straw.

DIFFERENTIAL DIAGNOSIS

The peptic ulcer should be differentiated from the other types of ulcer of the esophagus previously enumerated, which can be done as a rule quite readily by the history, by their association with other diseases, or by the laboratory findings. Due to the resemblance of the symptomatology, they may be confused with those of the stomach or duodenum, and especially with high-lying ulcers in the former, but at the same time, one should remember that these lesions may co-exist when only a very careful study may be able to distinguish the fact. Unless the roentgen examination can definitely indicate the site of the lesion, the esophagoscope, as so frequently is the case in this disease, must be relied on for the diagnosis.

Ulcers in the lower half of the stomach and those of the duodenum can usually be ruled out by the location of the pain, and often by the dysphagia so commonly present with esophageal ulcers.

Carcinoma of the esophagus does not early have as prominent a symptom of pain or tenderness, and is quite readily differentiated by the roentgen examination by the time that clinical symptoms are present. Bleeding from esophageal varices can be suspected from the history of liver cirrhosis or other disturbance of circulation, and by the absence of pain. Cicatrization from corrosives has a diagnostic history. Cardiospasm has a typical roentgenologic picture, and though ulcer is not considered an etiologic factor if, however, it is suspected, further proof can be had with esophagoscopy.

TREATMENT

Due to the evident association of peptic ulcer with infection, all foci of infection should be removed. The patient may respond readily to general peptic ulcer management, though it is more likely that these ulcers will be found resistant or recurrent. Topical application of 5 per cent silver nitrate or similar agents through the esophagoscope gives the patient such prompt relief that he is willing to forego any discomfort that may attend the treatment.

The number of treatments will vary with the case, usually from only a few in some to a large number in the most resistant types, and this may extend the treatment over several years before a complete cure can be effected. If medical management fails, or the dysphagia and pain are not controlled, a gastrostomy may be performed, which usually gives very prompt relief. This was seen notably in a case reported by Fleischner[2] which had resisted entirely very good medical treatment such as just described,

but became symptom-free and clinically well two months after a gastrostomy was done.

Though such a brilliant result is obtained by surgery, it seems that this procedure has enough risk attending its use to consider it indicated only after failure of the medical treatment. Hellmann, who is quoted by Fleischner, states that if an esophageal ulcer does not heal in a short time with the aid of medical and dietary treatments, a gastrostomy should be done.

PROGNOSIS

As the recognition of peptic ulcer of the esophagus increases clinically, we shall find that the prognosis is not as grave as it seemed to Tileston in 1906 when so many resulted in perforation and death. We find frequent mention of healed ulcers at postmortem examinations, so that we can assume they may heal spontaneously and when recognized more readily clinically and proper treatment instituted, we may speculate that the mortality for this lesion will be very low, and stenosis as a complicating resultant condition will also be rare.

SUMMARY

1. Peptic ulcer of the esophagus is a definite disease of frequent enough occurrence to be of real interest and importance. It has as its cardinal symptoms, pain, dysphagia, nausea and vomiting, and occasionally hemorrhage and perforation.

2. Its diagnosis calls for the closest cooperation between the clinician, the roentgenologist, and the esophagoscopist.

3. It has been infrequently diagnosed clinically in the past, but with development of the facilities for the roentgen examination and esophagoscopy, and if sought for in cases with substernal or epigastric pain, its incidence will be considerably higher than found heretofore.

4. The diagnostic criteria are yet incomplete and the roentgenologist has an important duty to perform in their further development.

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ROENTGEN-ANATOMIC STUDIES OF THE COLON IN SIX HUNDRED PATIENTS WITH PULMONARY TUBERCULOSIS

By HOMER L. SAMPSON *and* BÉLA HALPERT

Roentgen Laboratory, Trudeau Sanatorium
TRUDEAU, NEW YORK

Department of Surgery, Yale University School of Medicine
NEW HAVEN, CONNECTICUT

FOR several years past the writers have been collecting roentgen-anatomic data on the colons of patients with pulmonary tuberculosis. The aim was to discover: first, whether the colon shows by roentgenologic methods any characteristics peculiar to tuberculous individuals; and second, whether there are any roentgen-anatomic features of the colon peculiar to those individuals in whom intestinal tuberculosis has at any time complicated the pulmonary lesion. The data gathered suggest that there are no roentgen-anatomic features peculiar to tuberculous individuals nor is the colon different roentgenologically in patients in whom intestinal tuberculosis had complicated the pulmonary lesion from those in whom it did not. These conclusions, however, must not be regarded as final: first, because data similar to ours but on healthy non-tuberculous individuals are not available at present, and second, because the criteria used in the Trudeau Sanatorium for the diagnosis of intestinal tuberculosis are not as yet generally accepted.[2,10]

SEX AND AGE OF PATIENTS

In two preliminary communications the writers outlined their method of investigation and reported data on 300 patients.[3,8] In the present paper records on a similar series of 300 patients are presented and the findings in the total number of 600 patients, 300 of whom were male and 300 female, are summarized. Most of the patients studied were between twenty and thirty (172 male, 188 female), and between thirty-one and forty (89 male, 83 female) years of age. Only 34 (20 male, 14 female) were under twenty and 34 (19 male, 15 female) above forty, the youngest patient being fifteen and the oldest forty-nine years of age. Intestinal tuberculosis complicating the pulmonary lesion was clinically diagnosed in 36 (19 male, 17 female) of these patients.

All the data given refer, as before, to findings in the upright position and the roentgenograms mentioned are twenty-five hour films taken in the same position.

THE CECUM AND THE COLON ASCENDENS

The cecum was located in the *1st position*, i.e., near the crista iliaca, in 3 (all male), or 0.5 per cent of the 600 patients; in the *2d position*, i.e., in the fossa iliaca, in 118 patients (83 male, 35 female), or about 20 per cent; in the *3d position*, i.e., on the linea terminalis, in 285 patients (151 male, 134 female), or about 47 per cent; in the *4th position*, i.e., in the pelvis minor, in 194 patients (63 male, 131 female), or about 32 per cent.

The ascending colon was dextroconvex in all patients in whom the cecum lay in the 3d or 4th position; these groups comprised about 80 per cent of the total. In the rest the ascending colon was rather straight.

As before, the length of the ascending colon was considered average if the hepatic flexure was at the level of the third or fourth lumbar vertebra and the cecum in the 2d or 3d position respectively. Deviation from this group was considered long or short respectively.

The length of the ascending colon was *average* in 340 patients (164 male, 176 female) or about 57 per cent, *long* in 139 patients (61 male, 78 female), or about 23 per cent, *short* in 121 patients (75 male, 46 female), or about 20 per cent.

THE FLEXURA COLI DEXTRA

The hepatic flexure (flexura coli dextra) was located at the level of the fourth lumbar vertebra (L_4) in 301 (161 male, 140 female), or about 50 per cent of the 600 patients; in 191 (60 male, 131 female), or about 32 per cent, it was below (all at L_5), and in 108 (79 male, 29 female), or 18 per cent, above. Of those situated above the level of the fourth lumbar vertebra 87 (62 male, 25 female) were at L_3, 18 (14 male, 4 female) at L_2, and 3 (all male) at L_1.

In only 70 (46 male, 24 female), or about 12 per cent of the 600 patients, did the ascending colon turn into the transverse colon at approximately a right angle. In all the other patients the hepatic flexure was an acute angle. In 362 (175 male, 187 female) the first portion of the transverse colon lay parallel with the ascending colon: in 175 patients (101 male, 74 female) for half of the length or less, in 187 (74 male, 113 female) for more than half the length of the ascending colon. Out of the 362 patients in whom the transverse colon lay parallel with the ascending colon for any distance, the presence of adhesions about the hepatic flexure was inferred in 285 (151 male, 134 female), or about 48 per cent.

THE COLON TRANSVERSUM

In all but 4 (3 male, 1 female) of the 600 patients, the transverse colon was *caudo-convex*. Its bow was regular in 569 patients; in the balance, 31 patients (21 male, 10 female), its course was irregular. The irregularity occurred usually near the hepatic flexure, or the middle of the transverse colon.

THE POSITION AND THE RELATIVE POSITION OF THE TRANSVERSE COLON AND THE GREATER CURVATURE OF THE STOMACH

In all but 5 (3 male, 2 female) of the 600 patients, the transverse colon was at a lower level than the greater curvature of the stomach.

Perfect fusion, non-fusion, imperfect fusion and irregular fusion of the layers of the greater omentum were judged, as before, by the relative position of the stomach and the transverse colon as seen during roentgenoscopic examination, by palpation, and on roentgenograms.

A *perfect fusion* (1) of the layers of the greater omentum was inferred in 213 patients (148 male, 65 female), or about 35 per cent; a *non-fusion* (2), i.e., absence of the so-called gastrocolic ligament in 214 patients (73 male, 141 female), or about 36 per cent; an *imperfect fusion* (3) in 147 patients (64 male, 83 female), or about 24 per cent; an *irregular fusion* (4) was deduced in 21 patients (12 male, 9 female), or about 4 per cent. The 5 patients in whom the greater curvature of the stomach reached below the level of the transverse colon are, of course, not included in these figures.

The most dependent portion of the transverse colon was located above the level of the promontorium in 124 patients (96 male, 28 female), or about 21 per cent. In the rest, 476 patients (204 male, 272 female), or about 79 per cent, it reached below the level of the promontorium, in 98 of these (20 male, 78 female) even lower, i.e., about the level of the symphysis. Of the 124 patients, in whom the transverse colon was above the level of the promontorium, in 94 (69 male, 25 female) the lowest point of the convexity was located at L_5, in 19 (18 male, 1 female) at L_4, in 9 (8 male, 1 female) at L_3, in 1 (female) at L_2 and 1 (male) at L_1.

The lowest point of the greater curvature of the stomach was situated above the level of the fourth lumbar vertebra (L_4) in only 23 patients (19 male, 4 female), or about 4 per cent (18 at L_3 and 5 at L_2). In the rest, or 577 patients, the convexity reached lower than the level of the third lumbar vertebra (L_3). It was located in 110 patients (85 male, 25 female), or about 18 per cent, at the level of L_4, in 251 patients (135 male, 116 female), or about 42 per cent, at the level of L_5, and in 216 patients (61

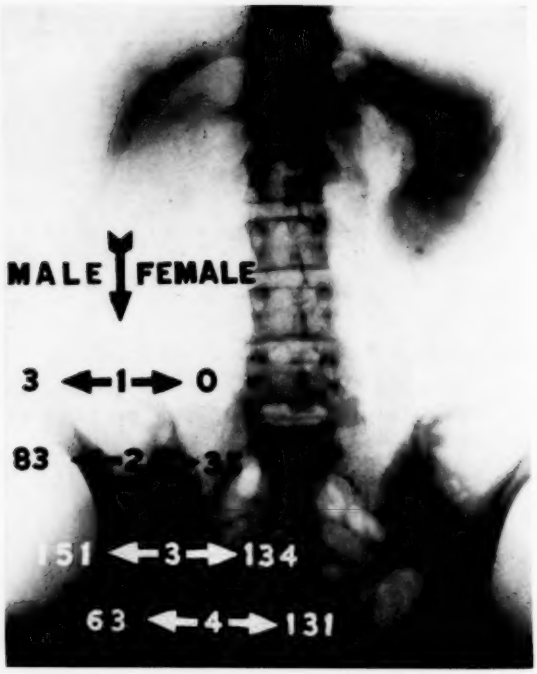

FIG. 1. Position of the cecum in relation to the skeleton. The cecum was located near the crista iliaca (1st position) in 1 per cent of the males; in the fossa iliaca (2d position) in about 28 per cent of the males and in only about 12 per cent of the females; on the linea terminalis (3d position) in about 50 per cent of the males and in about 45 per cent of the females; in the pelvis minor in 21 per cent of the males and in about 43 per cent of the females. Thus the usual position of the cecum in both sexes is on the linea terminalis; it is situated in the pelvis minor twice as frequently in females as in males.

male, 155 female), or 36 per cent, below the level of the promontorium.

THE FLEXURA COLI SINISTRA

In 89 patients (29 male, 60 female) the last portion of the transverse colon and the first portion of the descending colon did not contain sufficient barium to determine the position of the splenic flexure (flexura coli sinistra). In 236 (127 male, 109 female) or about 46 per cent of the remaining 511 patients the splenic flexure was located at the level of the third lumbar vertebra (L_3); in 124 patients (84 male, 40 female), or about 24 per cent, it was *above*, and in 151 patients (60 male, 91 female), or about 30 per cent, it was *below*. Of those patients in whom the splenic flexure was situated above the level of the third lumbar vertebra, in 100 (64 male, 36 female) it was located at L_2, in 19 (16 male, 3 female) at L_1, and in 5 (4 male, 1 female) at Th_{12}. Of those patients in whom it was situated below the level of the third lumbar vertebra, in 142 (58 male, 84 female) it was located at L_4, and in 9 (2 male, 7 female) at L_5.

The presence of adhesions between the transverse and the descending colon was inferred in 164 patients (72 male, 92 female or about 32 per cent of the 511 patients in whom the splenic flexure was properly outlined.

THE COLON DESCENDENS AND THE COLON SIGMOIDEUM

The descending colon and the sigmoid are not considered here in detail because in about half of the patients they were empty at the time of observation. Out of the 395 patients (221 male, 174 female) in whom the sigmoid contained some barium, a part of the sigmoid reached above the level of the transverse colon in 21 patients (6 male, 15 female).

ANALYSIS OF DATA ACCORDING TO SEX

All variations of the colon as to shape, position, peritoneal and topographic relations were encountered in both sexes. Striking differences were noted, however, in the frequency of their occurrence.

The *cecum* was located in the fossa iliaca in about 28 per cent of the males and in only about 12 per cent of the females. Except for the 1 per cent of the males in whom it was situated about the level of the crista iliaca, the cecum was in a lower position than the fossa iliaca, i.e., on the linea terminalis in about 50 per cent of the males and in about 45 per cent of the females, and in the pelvis minor in 21 per cent of the males and in about 43 per cent of the females. The usual position of the cecum in both sexes is thus on the linea terminalis; it is situated in the pelvis minor twice as frequently in females as in males. (Fig. 1).

The *ascending colon* was of average length in about 55 per cent of the males and in about 59 per cent of the females. It was longer in about 20 per cent of the males and in 26 per cent of the females, and it was shorter in 25 per cent of the males and in about 15 per cent of the females.

The *flexura coli dextra* formed an approximately right angle in only about 15 per cent of the males and in 8 per cent of the females. In the others it was an acute angle and the first portion of the transverse colon lay parallel with the ascending colon in about 34 per cent of the males and in about 25 per cent of the females for half of the length or less of the ascending colon, and in about 25 per cent of the males and in about 38 per cent of the females for more than half of the length of the ascending colon. The presence of adhesions about the hepatic flexure was inferred in about 50 per cent of the males and in about 45 per cent of the females. The hepatic flexure was situated at the level of the fourth lumbar vertebra in about 54 per cent of the males and in about 47 per cent of the females. It was located above this level in about 26 per cent of the males and in about 10 per cent of the females, and below the level of the fourth lumbar vertebra in 20 per cent of the males and in about 43 per cent of the females. The usual position of the hepatic flexure in both sexes is thus at the level of the fourth lumbar vertebra; it is situated below the level of the fourth lumbar vertebra about twice as frequently in females as in males.

The *transverse colon* was caudoconvex in all but 3 (1 per cent) of the males and 1 of the females. Its course was regular in all but 7 per cent of the males and in about 3 per cent of the females. Except for 3 (1 per cent) of the males and 2 of the females the transverse colon was at a lower level than the greater curvature of the stomach. The most dependent portion of the transverse colon was located above the level of the promontorium in 32 per cent of the males and in only about 9 per cent of the females. It reached below the level of the promontorium in the rest, or in 68 per cent of the males and in about 91 per cent of the females.

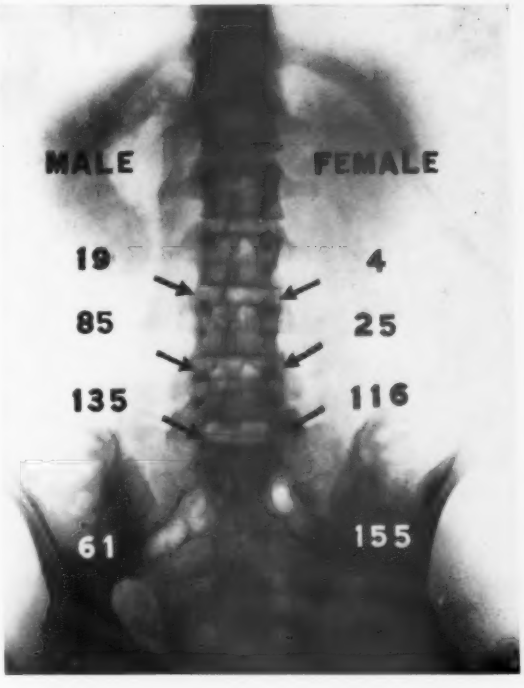

Fig. 2. Skeletal level of the lowest point of the greater curvature of the stomach. This point was located above the level of the 4th lumbar vertebra in about 6 per cent of the males and in about 1 per cent of the females; at the level of the 4th lumbar vertebra in about 28 per cent of the males and in about 8 per cent of the females; at the level of the 5th lumbar vertebra in 45 per cent of the males and in about 39 per cent of the females; below the level of the promontorium in about 20 per cent of the males and in about 52 per cent of the females. Thus the usual position of the lowest point of the greater curvature of the stomach in both sexes is at the level of the 5th lumbar vertebra; as a rule, it is found to reach lower in females by the height of the body of one vertebra, than in males.

The lowest point of the *greater curvature of the stomach* reached below the level of the third lumbar vertebra in about 94 per cent of the males and in about 99 per cent of the females. It was at the level of the fourth lumbar vertebra in about 28 per cent of the males and in only about 8 per cent of the females, at the level of the fifth lumbar vertebra in 45 per cent of the males and in about 39 per cent of the females, and

below the level of the promontorium in about 20 per cent of the males and in about 52 per cent of the females. The usual position of the lowest point of the greater curvature of the stomach in both sexes is thus at the level of the fifth lumbar vertebra; as a rule, it is found to reach lower in females by the height of the body of one vertebra (Fig. 2).

A *perfect fusion* (1) of the layers of the greater omentum was inferred in about 49 per cent of the males and in about 22 per cent of the females; *non-fusion* (2) i.e., absence of the so-called gastrocolic ligament in about 24 per cent of the males and in 47 per cent of the females; an *imperfect fusion* (3) in about 21 per cent of the males and in about 28 per cent of the females; an *irregular fusion* (4) was deduced in 4 per cent of the males and in 3 per cent of the females. According to the above data *non-fusion* of the layers of the greater omentum occurs about twice as frequently in females as in males.

The *flexura coli sinistra* was properly outlined in 271 of the males and in 240 of the females. Of these it was situated at the level of the third lumbar vertebra in about 47 per cent of the males and in about 45 per cent of the females. It was located above this level in about 31 per cent of the males and in about 17 per cent of the females, and below the level of the third lumbar vertebra in about 22 per cent of the males and in about 38 per cent of the females. The usual position of the splenic flexure in both sexes is thus at the level of the third lumbar vertebra, i.e., above the level of the hepatic flexure by the height of the body of one vertebra. The presence of adhesions between the transverse and the descending colon was inferred in about 27 per cent of the males and in about 38 per cent of the females.

The *descending colon* and the *sigmoid* were empty at the time of observation in about half of the cases. The sigmoid contained some barium in 221 males and in 171 females. Of these a part of the sigmoid reached above the level of the transverse colon in about 3 per cent of the males and in about 9 per cent of the females.

COMMENT

Our data are in many respects at variance with the current notions on skeletotopy (i.e., position of viscus in relation to skeleton) and syntopy (i.e., position of organs in relation to one another) of the abdominal organs. Responsible for the discrepancy is the fact that most of the available anatomic and roentgen-anatomic studies are not entirely free from some or all of the following objections: first, omission of consideration of the influence of posture upon the shape, position and topographic relations of the abdominal organs; second, designation of levels and distances by measures other than those furnished by the body itself; and third, lack of emphasis upon differences in the two sexes. To these it may be added that with the exception of a few investigators, the number of cases studied was too small for data to be of quantitative value.

In our series the first mentioned pitfall of error was avoided by taking all the final readings uniformly in the upright position of the subject, this being the only situation in which all the abdominal viscera naturally assume their lowest possible position. The second pitfall was avoided by expressing the levels and distances by means furnished by the individual's own skeleton. Finally an equal number of males and females of approximately the same age were studied and the data kept apart.

All individuals included in our series had or were suspected of having, clinical pulmonary tuberculosis. The individual variations in both sexes and the differences observed between the two groups were, however, so ample that we venture to suggest that if data comparable to ours were collected on healthy, non-tuberculous individuals, the results would closely resemble those here presented.[6,7,11]

Efforts should be made to supplement and, whenever practicable, to verify the roentgenologic data on the living by ap-

propriate anatomic investigations. Particular emphasis should be laid upon fusions between the layers of the greater omentum and upon additional but not necessarily pathologic connections between parts of the colon.* Data of this nature will go far in correlating structure with function and in clarifying clinical conditions attributed to malposition.[2,1,5]

SUMMARY

Roentgen-anatomic studies on the colons of 300 male and 300 female patients with pulmonary tuberculosis are reported. The data given refer especially to the skeletal position of the cecum, length and shape of the ascending colon, shape and skeletal position of the hepatic flexure, transverse colon, splenic flexure, descending colon and sigmoid, and also the skeletal position of the greater curvature of the stomach in the upright position.

The usual location of the *cecum* in both sexes was on the linea terminalis; it was situated in the pelvis minor twice as frequently in females as in males.

The usual location of the *hepatic flexure* in both sexes was at the level of the fourth lumbar vertebra; it was situated below this level about twice as frequently in females as in males. Adhesions between the ascending and the transverse colon were inferred in about 50 per cent of the males and in about 45 per cent of the females.

The most dependent portion of the *transverse colon* reached below the level of the promontorium in 68 per cent of the males and in about 91 per cent of the females.

The usual position of the lowest point of the *greater curvature of the stomach* in both sexes was at the level of the fifth lumbar vertebra; as a rule it was found to reach lower in females by the height of the body of one vertebra, than in males.

Non-fusion of the layers of the greater omentum, i.e., absence of the so-called gastrocolic ligament, was inferred about twice as frequently in females as in males.

The usual position of the *splenic flexure* in both sexes was at the level of the third lumbar vertebra, i.e., above the level of the hepatic flexure by the height of the body of one vertebra. Adhesions between the transverse and the descending colon were inferred in about 27 per cent of the males and in about 38 per cent of the females.

The data gathered suggested no roentgen-anatomic features peculiar to tuberculous individuals, nor was the colon different roentgenologically in patients in whom intestinal tuberculosis had complicated at one time or another the pulmonary lesion from those in whom it did not.

* A paper by Samuel C. Harvey[4] contains a comprehensive analysis of the peritoneal relations of the colon and a critical review of all the literature up to date (1918).

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CLEIDOCRANIAL DYSOSTOSIS

REPORT OF A CASE*

By R. N. KLEMMER, M.D., PAUL O. SNOKE, M.D., *and* H. K. COOPER, D.D.S.
LANCASTER, PENNSYLVANIA

CLEIDOCRANIAL dysostosis is one of those peculiar clinical entities, congenital in origin, which has always aroused the interest of the physician. Although a few cases were reported earlier, this condition did not receive general attention until it was described and named hereditary cleidocranial dysostosis by Marie and Sainton[10] in 1898. It was in the following year that Terry[20] reported his studies upon an anatomical preparation of such an individual.

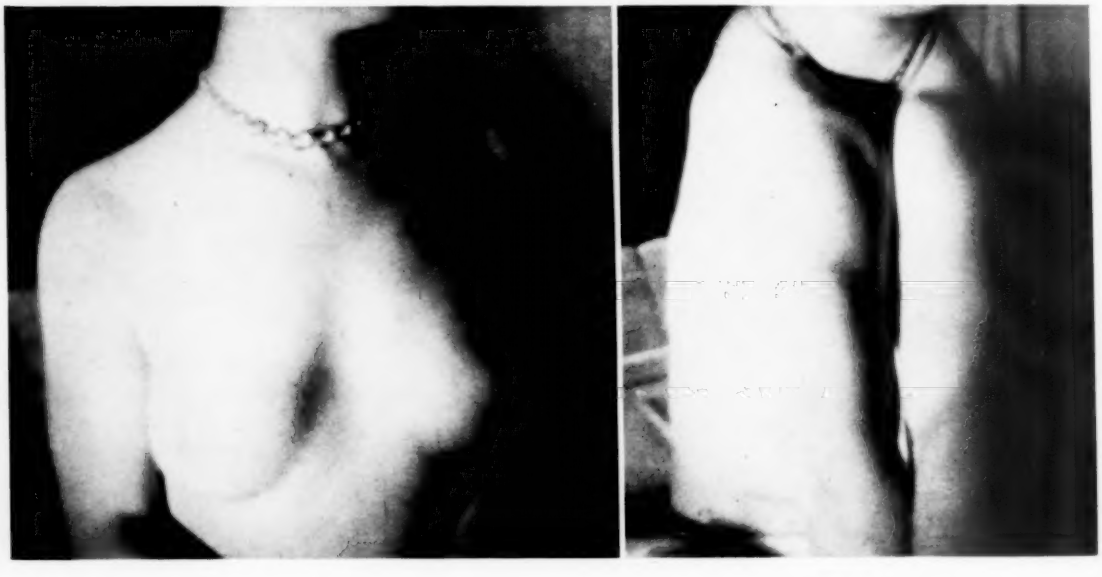
By common consent, it is generally considered that a congenitally defective clavicle is the sine qua non of the condition. This defect may vary from the presence in the shaft of a thin fibrous section which can be diagnosed with confidence only from the roentgenogram, and then resembles an ununited fracture, to the complete absence of both clavicles. At least one case has been reported where the clavicular defect was the only one found.

The striking condition of late closure or even premanent patency of the fontanelles with wide suture lines and numerous Wormian bones is frequently associated with the clavicular deformity.

Prolonged retention of deciduous teeth, faulty implantation and delayed eruption of the permanent teeth with enamel defects are frequently noted.

Careful study, especially by means of the roentgen ray, has revealed many other anomalies, the number of these apparently varying with the thoroughness of the examination and the keenness of the observer.

We wish to report a case of this dysostosis because of its rarity.



A B

FIG. 1. A. Normal posture. B. Shoulders approximated anteriorly. (Enlargement from 16 mm. motion picture film.)

* Reported through the courtesy of Dr. J. T. Herr, Landisville, Pa. Presented at the December, 1930, meeting of the Philadelphia Roentgen Ray Society.

CASE REPORT

Annabelle S., aged fifteen. She is a perfectly healthy girl who is in the ninth grade at school. She has had practically no illnesses. She indulges freely in tennis and swimming without any ill effects. Her father, mother, two brothers and two sisters are all healthy and no members of the family are known to have defective clavicles or abnormal dentition.

She appears well nourished but is about 12 pounds below her average weight. She walks rather stiffly erect with most of her weight upon her heels as if on stilts. There is a tendency to brachycephaly and the two frontal bosses are moderately prominent. The anterior and posterior fontanelles are about one-half inch in diameter. The normal width of her shoulders is 12¾ inches but she can very readily approximate the deltoid eminences anteriorly, thereby decreasing the shoulder width to 5¾ inches (Fig. 1). The clavicles are absent except for bilateral stumps, each 2 inches in length and attached to the sternum. Fingers and toes are short and tapering. Secondary sexual characteristics are very well developed.

Roentgenograms reveal the following anomalies:

Skull: The bregma is open and extending anteriorly from it there has been failure of ossification along the line of the sagittal suture, over a wide area. There is an osseous defect of considerable size in the right supraorbital ridge (Fig. 2). The asterion is open. All sutures are wider than normal. Although the patient is fifteen years of age, many of the deciduous teeth are still present and the numerous permanent teeth are unerupted and malposed.

Fig. 2. Note open bregma and anterior sagittal suture; also defect in right supraorbital ridge. The asterion is open and all sutures are prominent.

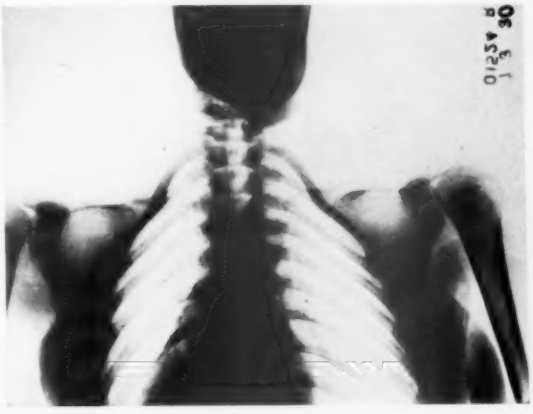


Fig. 3. Note sternal stumps of clavicles and deformity of scapulae.

Clavicles: Both clavicles are absent. The only remaining vestiges are the conical sternal stumps, which are about 2 inches long with rounded tips, In spite of the absent anterior arch of the shoulder girdle, the shoulders maintain their normal level. The ribs show a wave-like deformity frequently noted following rickets. A very obtuse angle with the spine is formed by the ribs, lending a cone-like appearance to the chest.

Scapula: The supraspinous fossa is absent. The root of the scapular spine forms the upper border of the scapula (Fig. 3).

Hands: The metacarpals are normal in length but the shafts show distinct narrowing, especially in the region ossified earliest, i.e., near the proximal ends of the second, third, fourth and fifth, and the distal end of the first, while the opposite ends of the bones are normal. The cortex is very dense in these constricted areas but elsewhere there is a tendency to cortical thinning.

The proximal row of phalanges shows similar changes, except that the constricted regions are in the distal portion of all of the shafts.

The middle row of phalanges is foreshortened, being about one-half of the normal length. They are consequently thick and stubby. The terminal phalanges are spear-point in type and several are foreshortened. The hand is pudgy.

FIG. 4.

Wrist: The carpus shows nothing of note.

Radius and Ulna: Only the lower ends were examined and it was noted that the styloid processes were on the same level, whereas normally the radial styloid is lower than the ulnar (Fig. 4).

Feet: The deformities previously noted in the hands are reproduced in the metatarsus and phalanges. In addition we find a marked outward sweep of the metatarsus as frequently seen in talipes cavus. This is due to a very high anteroposterior arch.

The tarsus reveals an inadequately developed astragalus and calcaneus (loss of quantity). The astragalar neck is very thin. This failure in development of the heel causes marked foreshortening which throws the line of weight-bearing far posteriorly so that we almost have talipes calcaneo-cavus. This accounts in large measure for the patient's peculiar gait (Fig. 5).

We regret that studies of the knees, pelvis and other views of the skull were not obtained.

DENTAL CONSIDERATIONS

Hereditary cleidocranial dysostosis manifests itself from a dental standpoint in the delayed eruption of the teeth. However, it usually seems to affect only those teeth that have deciduous predecessors.

For years there has been much speculation and many theories as to the process of the eruption of teeth, and dental literature has devoted much space to this subject, yet the mechanism by which teeth find their way into proper position and stop there is far from being understood.

Some teeth are delayed in their eruption due to mechanical causes; in other words, they are late coming in because they have met with an obstruction in finding their way into the arch. For example, the cuspid teeth have to travel some distance from where their development begins and they must pass between the lateral incisors and the first bicuspids. Very frequently there is not sufficient room for them to do this and they either remain in the jaws or erupt on the buccal or palatal side of the arch. We are not certain of the cause for the delayed eruption of the teeth in cleidocranial dysostosis. We know that in this disease the bones laid down in membrane, wholly or partially, are the ones particularly affected.

A

B

FIG. 5.

We also know that, after the clavicle, calcification occurs next in the mandible and then in the maxilla. Whether this fact has anything to do with the delayed eruption of the teeth or the non-eruption of the teeth is problematical.

It has been suggested by some that the disease is due to the absence of certain chemical constituents for correct ossification and it may be looked upon as a deficiency disease, possibly due to interference with calcium metabolism.

Figure 6 is a photograph of a plaster cast of our patient's mouth illustrating the non-eruption of the permanent teeth. The thickness of the gums above the upper anterior teeth shows the pressure of the permanent teeth.

Fig. 6. Dental cast of teeth.

EMBRYOLOGY

Piersol[15] states that the clavicular center in the embryo is laid down before all others, being evident at the sixth week. The cartilaginous outline appears later and ossification begins shortly thereafter. The center of the shaft ossifies first. If therefore we wish to find the etiological factor in these cases we must go back to the sixth embryological week.

We secured several embryos from the collection in the museum of the Lancaster General Hospital and submitted them to roentgen examination. The first one was sixteen weeks old and here we found the clavicles ossified and well developed. The second embryo was less than eight weeks old. We saw no evidence of calcification anywhere. The shoulder girdle was visible but only cartilaginous.

ASSOCIATED DEFECTS REPORTED IN THE LITERATURE

These are so numerous that only a brief synopsis can be given. The facial skeleton is frequently smaller than the cranial. The frontal, parietal and occipital bosses are often unduly prominent. The lower jaw is commonly prognathous. The face is often small, both absolutely and relatively, in comparison with the head. The suborbital region may be shrunken and depressed. There may be a marked constriction of the maxillary region of the upper face. The bridge of the nose may be sunken due to defective formation or even absence of the nasal and lacrymal bones. The zygomatic bones may be very small or otherwise defective and the superior maxillae are often small. The sinuses may be small or certain ones may be absent. A high arched palate is very frequent and cleft palate sometimes occurs. Cases have been reported with general contraction of the base of the skull and a saddle-shaped formation of the transverse diameter or the tilting forward of the foramen magnum so that it pointed toward the frontal bones. Cervical ribs are common. The scapulae, spinal column, thorax and pelvis may be deformed. Kyphosis, lordosis, and scoliosis are frequent. Spina bifida has existed in this condition. The pelvis may be so contracted that cesarean section is necessary for delivery.[11]

Coxa vara or genu valgum is noted in many cases, sometimes requiring corrective osteotomy. Foreshortening of the os calcis was noted in our case. Shortening of the phalanges is frequent and in a number of cases, including our own, spear-pointed distal phalanges of the fingers and toes were observed (Figs. 4 and 5). The defects of

fingers and toes have been so frequent that several authors have called their cases cleidocranio-digital dysostosis.[13,16]

Anomalies of other structures than the bony skeleton seem rare. Of course anomalous muscle and tendon attachments accompany the bony defects. Slight and moderate disorders of thyroid function, particularly hypothyroidism, seem rather frequent.

Brain lesions are occasionally reported. McCurdy and Baer[9] report a mentally deficient negro with congenitally defective clavicles. A demented female with slight spastic paralysis of the lower limbs associated with cleidocranial dysostosis is reported by Stewart.[17] Pathological reports of examinations on the nervous system are few. Stewart's case at necropsy showed old inflammatory lesions of the brain, extremely small frontal lobes and other structural anomalies of the central nervous system.[18] The case autopsied by Léri and Trétiakoff[8] showed inflammatory and hemorrhagic lesions of the brain. In Marie and Sainton's first case a large syringomyelia was present. In one case cavities the size of pigeon eggs were found in each frontal lobe.[10] These inflammatory lesions and possibly also other structural brain anomalies we believe may best be explained as having a separate etiology from that of the clavicular defects. Stocks[19] and more recently Fitchet[3] have made excellent studies of this disease and have compiled a careful bibliography. We would submit the following additional references.[1,2,6,7,12]

HEREDITARY FACTORS

This condition is frequently but not necessarily hereditary. It may be transmitted by either parent to either sons or daughters. It was formerly believed to be limited to two generations but there are reliable reports of the anomaly passing through three[6] or even four[3] generations.

We believe that the hereditary element cannot be ruled out except by roentgenograms of the shoulder girdles of all the members of the immediate family. These defects may be so slight that they will escape detection during a physical examination, or the examiner may erroneously consider the deformity consequent upon fracture.

ETIOLOGY

The etiology is speculative. Jansen[5] suggested that a small amniotic membrane with hypertension of the amniotic fluid pressing on the embryo at about the eighth week of pregnancy caused the condition. This explanation seems untenable. Hultkrantz,[4] Paltauf,[14] and others, believe that the fault lies in a primary change in the parental germ plasma. The syndrome strikingly concerns the bones developed from membrane such as the clavicles and the bones of the cranium, and yet defects of other bones are frequently associated The shaft of the clavicle is developed from membrane while the distal extremities arise from cartilage. We fi[illegible] the clavicular defect is usua[illegible] whole clavicle may be ab[illegible]de sutures and open fontanelles are not due to an abnormally large brain b[illegible]o retarded growth of the bones of the cranium. Cleidocranial dysostosis is closely related to, and must be distinguished fr[illegible]m, achondroplasia and rickets. The distinction is easy because neither of the la[illegible]r diseases has defects of the clavicles. However, many of the secondary features of cleidocranial dysostosis are so similar to rickets that certain investigators have considered that the latter condition almost constantly accompanies defective clavicles and therefore accounts for many of the findings in this clinical entity. Kelley[6] suggests that cleidocranial dysostosis is an abnormal condition inherited as a dominant Mendelian factor, and is a mutation of recent origin. This seems to be a logical conclusion.

SUMMARY

1. An additional case of cleidocranial dysostosis is reported, with roentgen studies of obviously deformed skeletal struc-

tures. We believe that complete roentgen studies are advisable in all such cases.

2. The hereditary factor seems to be absent in our case but this cannot be considered as proved because roentgen studies of other members of the family were not permitted.

3. No therapy is indicated for uncomplicated cases of cleidocranial dysostosis. Frequently, however, they require the attention of an orthodontist to mitigate dental difficulties, and occasionally some of the numerous skeletal abnormalities may cause sufficient functional disturbance to necessitate surgical intervention.

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THE ROENTGEN-RAY TREATMENT OF EXPERIMENTAL TUBERCULOSIS*

By JOHN W. SPIES, M.D.
Department of Surgery, Yale University School of Medicine
NEW HAVEN, CONNECTICUT

INTRODUCTION

THE effect of roentgen rays upon infectious processes has been of only slightly less interest than that manifested as to their action in neoplastic diseases. Many clinical and laboratory studies have been made, and in the latter the susceptibility of the organisms to roentgen rays has been observed both in vitro and in vivo. In order that the former might be more accurately evaluated, various techniques and their application have been reported, among the recent ones being that by Lacassagne[19] and its elaboration by Mme. Curie.[6]

Although the influence of the roentgen rays upon pyogenic infections has been the subject of numerous communications (Belot[4] and others), its action on tuberculosis has perhaps aroused a keener interest.

Grasset[11] attempted to show that there might be some correlation deduced between the in vitro and in vivo studies because, whether they were in or out of the body, there remained some similarities in the morphology and staining reactions of the organisms.

Lange and Fraenkel[20] stated that the roentgen rays might kill tubercle bacilli disposed in thin layers, but that such an effect was to be hoped for only in cultures at least four or five weeks old. They thus assumed that the behavior of the tubercle bacillus toward roentgen radiation was contrary to the Tribondeau-Bergonié Law which held that the susceptibility of cells should vary inversely with the age. However, this rule was formulated for animal tissues and not for bacteria.

As a result of carefully controlled work, Haberland and Klein[12] decided that roentgen rays had no effect on the tubercle bacillus in vitro, and that any good results from therapy must be due to the reaction of the host and not to any direct effect upon the bacteria. The idea that radiation did produce a demonstrable general change in the tissues was supported by numerous investigators, among them being Mendeléeff,[26] who reported that it caused an alteration in the blood serum of a guinea pig, which was evinced by increased mitosis of the skin and intestine immersed in it. Nasta, Jovin, and Blechmann[30] thought that guinea pigs inoculated with tubercle bacilli and then irradiated with roentgen rays showed less reaction to tuberculin (intracutaneous and intraperitoneal) than did the controls. Abramowitsch and Rabuchin[1] decided that a change was seen in the intensity of the tuberculin reaction either when the tuberculin was irradiated in vitro or the skin at the site of injection had been previously subjected to roentgen irradiation.

Murphy and Ellis[29] found white mice to be more susceptible to bovine tuberculosis after exposure to roentgen radiation and thought that their lowered resistance to the disease was probably due to a destruction of the lymphocytes. Morton[27] described a rapid diagnostic test based on the increased sensibility of guinea pigs to tuberculosis after irradiation. Baeuchlen[3] at a later date found a diminution in the number of lymphocytes and a relative increase in the polymorphonuclear neutrophiles. On the other hand, Kellert[13] advanced the idea that the good effects reported by early investigators might have been due to small doses stimulating the lymphocytes. Epstein[8] concluded from a review of the literature, and from a series of his own experiments de-

* This study was begun in the University of Louvain, Belgium, while the author was a joint fellow of the C. R. B. Educational Foundation, Inc. and the Memorial Hospital of New York City, and was completed as a member of the Department of Surgery, Yale University School of Medicine, New Haven, Connecticut.

voted to the study of the blood cells in guinea pigs, that the lymphocytes have no effect on tuberculosis; and that, although the formation of antibodies was hindered, those already formed were not affected by the roentgen rays.

The above considerations, purporting to show that general effects are produced by roentgen radiation should be kept in mind, because Krause,[15] Willis,[42] Valtis,[41] Martenstein,[24] and others, have demonstrated that the tubercle bacillus may migrate from the local site of injection to the regional lymph nodes within a few hours and thence into the systemic circulation within a few days. Consequently, any therapeutic agent should be germicidal and be applied early, or else have a widespread effect, in order to influence the disease.

Reports dealing more directly with the results of roentgen therapy in experimental tuberculosis have been numerous, and their conclusions have been greatly at variance.

For example, Baeuchlen[3] thought that tuberculosis in rabbits was not favorably influenced by roentgen radiation. Although there was evidence of healing in the peripheral lymph nodes, the lesions in the viscera seemed to be more widespread than in the controls. Microscopically, he could detect no difference in those irradiated or not. In a small series of guinea pigs, Lortet and Genoud[21] found that the controls had abscesses of the regional lymph glands, whereas the nodes of the irradiated animals were hard and circumscribed as a result of fibrosis. Muehsam[28] concluded that roentgen rays did not prevent the generalization of the disease in guinea pigs but did reduce the size of the local lesions. Rodet and Bertin-Sans[36] thought that in no case did their animals receive benefit from the treatment. Ogus[31] inferred the opposite, but she admitted that the roentgen rays had a deleterious influence upon the nutrition of the animals. One of the early reports came from Fiorentini and Luraschi[9] who stated that roentgen rays produced a favorable action upon peritoneal tuberculosis of guinea pigs. At a much later date, Ford[10] was unable to confirm this and thought that perhaps the opposite was true. Schroeder[37] injected rabbits with a bovine strain of tubercle bacillus and expressed his opinion that large doses of roentgen rays should be used, since, although they had no effect on pulmonary tuberculosis, they did have a favorable one on the involved, local lymph glands. Ritter and Moje[35] studied the effects of roentgen therapy upon the tuberculosis of guinea pigs, which had been intracutaneously inoculated in the groin. Except for the lack of controls, their experiment was well planned. They affirmed that the tubercle bacillus per se was relatively insusceptible to roentgen energy and indicated that a favorable influence was obtained through a stimulation of connective tissue growth and of phagocytosis, but that it was harmful to employ large doses.

From the above, and from many reports not quoted, one is inclined to the view that if there are beneficial results to be derived from the roentgen therapy of tuberculosis, such is observed only in the infected, superficial lymph nodes or skin.

The following clinical reports have been reviewed in order to demonstrate that these effects may also be hoped for in human patients. It should be remembered then that the ones to be cited deal with tuberculous, cervical lymphadenitis; and that, whereas they are indicative of the general trend of opinion, contrary notions have been expressed by certain authors.

Boggs[5] claimed a cure for over 90 per cent of his cases and thought that the usual lack of recurrence was due to an immunity being conferred by the radiation. Marian,[22] Disson,[7] and Pfahler,[33] believed the roentgen ray to be a satisfactory agent, but the last named warned against its use in the hands of the incompetent. Wyss and Eghiayan[44] obtained good results except where there was preëxisting, marked fibrosis of the lymph nodes. Stettner,[38] Wilms,[43] Tichy,[40] Kneier,[14] Thiemann,[39] and Peyser[32] each considered roentgen therapy to be the method of choice. Reyn[34] was not so enthusiastic and warned against the use of in-

jurious doses. Markus[23] regarded the treatment as being highly beneficial, but likewise advised against possible damaging effects to the patient.

PURPOSE OF PRESENT STUDY

From this brief, incomplete perusal of the literature, one may see that the roentgen therapy of tuberculosis has aroused great interest, and that only in its application to involved cervical lymph nodes, and perhaps to the skin, have reports very consistently justified its continued usage. The seeming variance between the results obtained by those dealing with the experimental forms reasonably entitled one to re-attack the problem. In doing so, it appeared desirable to transfer to animals the technique used in the clinic. Such was the aim of this investigation.

EXPERIMENTS

Animals

One hundred and fifteen guinea pigs and eight rabbits were employed. All were healthy young adults. Their reaction to tuberculin was not tested, as it was felt that the condition of the regional lymph nodes would be a sufficient index as to whether the organism came from the site of inoculation, and that small discrepancies could be ruled out by a sufficiently large series.

Infecting Organisms

Two strains of human tubercle bacilli were kindly supplied by the University of Louvain Medical School, Department of Bacteriology. These had been studied for a long time, and it was known that one was scarcely virulent while the other was extremely so.

The preparation of the organisms for inoculation was as follows: A three to four weeks' culture was dried, placed in a mortar, and thoroughly ground with a pestle. Then normal saline was added, drop by drop at first, while the grinding was continued. After 2 or 3 c.c. of the saline solution had thus been run in, 0.5 c.c. was added at a time until the total reached approximately 10 c.c. The emulsion thus obtained was centrifuged for fifteen minutes at moderate speed, or until the density was uniform throughout, and a smear showed the bacilli to be evenly separated from one another. In each of two bottles, one-half ounce size, were placed 10 c.c. of fresh, clear, normal saline solution. Into one bottle was dropped bacterial emulsion until the very faintest detectable opalescence appeared, as compared to the saline solution in the other bottle. One cubic centimeter of this organism containing fluid was arbitrarily designated as a "unit," and by diluting with the proper amount of normal saline solution any desired fraction of a unit could be obtained in 1 c.c. of the diluent, 1 c.c. being the exact amount of fluid always injected.

I am indebted to the University of Louvain Medical School, Department of Bacteriology, for knowledge of the above method. The procedure was simple and yet permitted the giving of a uniform dosage of any desired strength.

Inoculations

Immediately after preparation of the tubercle bacilli, *intracutaneous* injections were made over the area of the ninth rib in the left midaxillary line, the hair from which had previously been removed by shaving.

The rabbits were used as a general check. In injecting them with a human strain of the tubercle bacillus, it was supposed very unlikely that they would become infected; and that, if they did, it would probably be due to an increased susceptibility following exposure to roentgen rays, or else that a large dose of the very virulent organisms had overcome their normal resistance.

Irradiation

In the Radiotherapy Clinic of the University of Louvain Cancer Institute tuberculous glands of the neck have been successfully treated by roentgen rays. As a rule, 8 weekly exposures have been given accord-

TABLE I

DOSAGE OF ORGANISMS

Guinea pigs		
Units	Number of Irradiated Animals	Number of Controls*
	Scarcely Virulent Tubercle Bacilli	
0.001	8	4
	Very Virulent Tubercle Bacilli	
0.1	4	2
0.01	8	6
0.001	7	7
0.0001	18	11
0.00001	∞	∞
0.000001	24	16
Total	69	46
	Rabbits	
0.001	4	4

* The word "control" is used in the sense that the animal was inoculated with tubercle bacilli but received no radiation.

ing to the following technique: kilovolts, 140; milliamperes, 4; filtration, 0.3 centimeter of copper; and skin-target distance, 30 centimeters. According to actual measurements, in one minute the above set-up delivered radiant energy to the amount of 100 R (French). The usual exposure was for 7 minutes; thus in each treatment the patient received upon the skin 700 R (French) units of roentgen energy. The Coolidge and Phillips models of roentgen tubes were employed. The above technique was the one used in the present investigation.

The animals were placed upon a suitable board with their limbs secured in such a manner that the left chest and axilla would be directly exposed to the roentgen rays. The other portions of the body were covered with leaded rubber.

Roentgen Exposures

These were made according to four different plans. In every instance, each irradiated animal was re-exposed to the roentgen rays at exactly seven day intervals, and each exposure lasted precisely seven minutes. Except where indicated in Plan No. 2, (a), the extremely virulent strain of tubercle bacillus was used for the inoculations.

Plan No. 1. Three guinea pigs were irradiated eight times. Then they and 3 others (not irradiated) were inoculated, following which they were subjected to no further procedures.

Plan No. 2. Timed from the day of inoculation, 8 guinea pigs were irradiated the day before, 8 others the same day, 8 additional ones the following day, and 8 more seven days after. All received seven subsequent exposures, making a total of 8. (a) Two guinea pigs out of each of the above four groups were inoculated with the scarcely virulent strain of tubercle bacillus, and a total of four controls was placed with them. (b) The remaining six in each lot were injected with the extremely virulent strain of Koch's bacillus, and 16 controls were allotted to them. Thus a total of 52 guinea pigs was employed in Plan No. 2.

Plan No. 3. (a) Timed from the day of inoculation, 11 guinea pigs were exposed to roentgen rays the day before and 11 others the same day. Subsequently, 7 irradiations were given, making a total of 8. Fifteen guinea pigs were used as controls; i.e., injected but not irradiated, making a total of 37. (b) Two rabbits were given radiation the day before and two others on the same day of inoculation. Seven other roentgen exposures were received, amounting to 8 in all. Four rabbits were used as controls, making a total of 8.

Plan No. 4. Timed from the day of inoculation, 6 guinea pigs were irradiated the day before and 6 others on the same day. One subsequent exposure was made, making a total of 2. Eight guinea pigs were used as controls, amounting in all to 20.

RESULTS

At least once each week the animals were examined as to general condition, reaction

at the site of inoculation, and the character of the regional lymph nodes. Autopsies were eventually performed on all. If the gross findings at necropsy seemed negative, smears from various organs were made, and the spleen was used to inject fresh guinea pigs and to make cultural studies. Otherwise, material was saved for microscopic section only. If the histologic examination disclosed no frank tuberculous lesions, the sections were stained for acid fast bacilli. By the use of the above procedures the absence or presence of tuberculosis was satisfactorily established in all of the animals.

According to these criteria none of the 8 rabbits inoculated with the extremely virulent strain of human tubercle bacillus nor any of the 12 guinea pigs injected with the scarcely virulent strain of human tubercle bacillus revealed any anatomic or bacteriologic evidence of infection.

The results found in the remaining 103 guinea pigs are given below. These were analyzed according to the amount of organisms inoculated and the plan of irradiation employed.

EFFECTS OF ORGANISMS

In the doses used, the larger the quantity of tubercle bacillus given to the animal, the shorter was its remaining duration of life. When fractions of units amounting to more than 0.0001 were given (see Table 1) the extent and frequency of ulcer formation at the site of inoculation varied directly with the amount of organisms delivered into the skin. The regrowth of hair was not affected except immediately over the area of ulceration. As a rule, when the animals came to necropsy, their tuberculous lesions were of the same extent despite the variance in dosage. However, it was stated above that the animals came to necropsy at a later date when the smaller amounts of the tubercle bacilli were given. The longer span of life would necessarily give more time for the spread of the disease, other factors being the same. In all probability, an animal dying of tuberculosis did so because the lesion had reached a certain form or extent, regardless of whether it had taken weeks or months.

EFFECTS OF IRRADIATION

In the present study the exposure of the animals to roentgen rays had no effect upon its remaining duration of life or upon its general condition while living. When doses of 0.0001 unit, or less, were given (see Table 1), the formation of ulcers was not seen in the controls, but a few were noted in the irradiated animals. The apparently normal return of the hair, which had been shaved from the site of inoculation, was taken to be indicative of mild treatment. Autopsies revealed no difference in the extent of tuberculosis whether the guinea pigs had been subjected to the roentgen rays or not.

In the animals receiving radiation during the eight weeks before inoculation (Plan No. 1), the enlargement of the lymph glands was at first retarded, but later the nodes increased until they were the same size as in the controls, and at necropsy the findings were similar. However, the number of pigs in this series was too small to permit of any positive deductions.

In irradiation Plan No. 2 no uniform difference could be detected between the various irradiated groups as compared to themselves or to the controls.

In Plan No. 3 there were likewise no consistent variations in the groups subjected to roentgen therapy when measured against one another and the controls.

In Plan No. 4 every guinea pig which was irradiated the same day that it was inoculated with tubercle bacilli, exhibited an early enlargement of the regional lymph nodes simultaneous with abscess formation and ulceration at the local site of inoculation. In neither the animals irradiated the day before injection nor in the controls were there such findings. Although further confirmation is needed before a positive statement is rendered, it would seem that the first irradiation given immediately after inoculation promoted the formation of local abscesses and ulcers, and

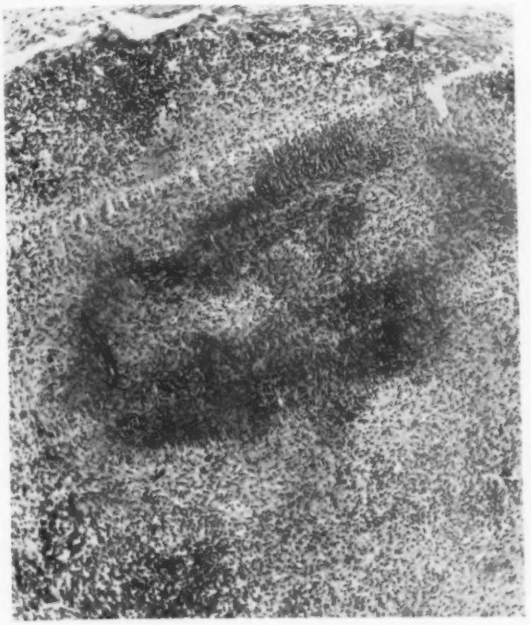

Fig. 1 (×85). This illustrates a caseous form of tubercle in which giant cells are absent, and lymphocytes and unidentified histiocytes are invading the necrotic areas and the newly formed connective tissue.

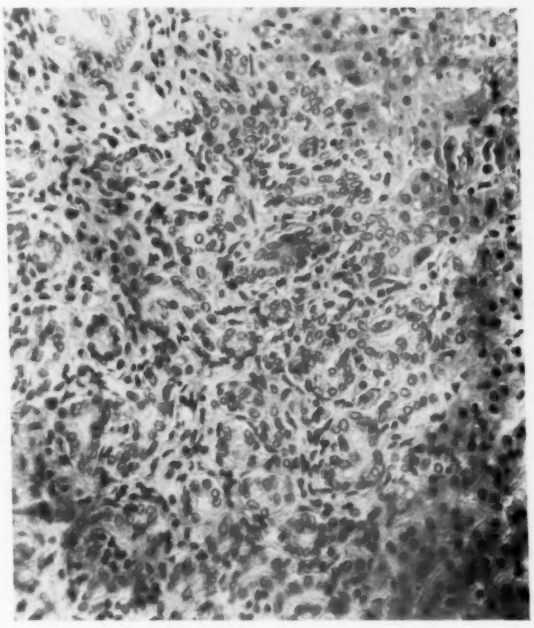

Fig. 2 (×250). This depicts a proliferative, tuberculous, hepatic cirrhosis. Bile ducts are to be seen in the lower and left-hand portions. Viable and degenerating liver cells may be perceived along the right-hand border of the photomicrograph.

that such formation was inhibited when sufficient, subsequent irradiations were given. The deduction is drawn from comparing the results in Plan No. 3 with those in Plan No. 4. The only difference between these two experiments was that in the former the radiation was delivered for eight successive weekly intervals, whereas in the latter only two exposures were given.

However, the marked local differences did not seem to have a great effect on the duration of life, for the ones that had the abscesses, ulcerations, and early enlargement of the lymph glands lived an average of 132 days after inoculation as compared to 116 days in the group irradiated before the day of the injection and 121 days for the controls.

HISTOLOGIC FINDINGS

There were four points of interest. First, there was a slight increase of the subcutaneous connective tissue in the irradiated area. This was observed in animals living for two months or more after the beginning of irradiation. Second, there was an almost total absence of giant cells (Fig. 1) and the rare ones seen were imperfectly formed. Third, the tubercles were of two distinct types: the proliferative, characterized by fibroplasia and invasion by "wandering" cells; and caseous, featured by collections of amorphous cellular débris. The former predominated in the lungs, and the latter was more prevalent in the spleen. Fourth, a marked cirrhosis of the liver was frequent. The organ was of normal size, had decreased flexibility, and many areas exhibited a grayish luster. The microscope revealed a moderate to extensive destruction of liver cells and their replacement by connective tissue and endothelioid cells. The process was essentially an extensive form of the proliferative type of tuberculosis (see Fig. 2).

DISCUSSION

A review of the literature reveals that the roentgen irradiation of human tuber-

culosis has apparently been a failure except in the involved skin and superficial lymph glands. These clinical observations have to a certain extent been borne out by experimental work, but it has been very difficult to secure analogous conditions in the animal as compared with those in man. One may easily see that, whereas the course of tuberculous cervical lymphadenitis in the human is a relatively chronic and benign affair, in the animals inoculated with tubercle bacilli the progress of the disease is acute and malignant. There is, consequently, a crying need for the production of a form of tuberculous adenitis in the cavy similar to that which spontaneously exists in the genus *homo*. This has been realized with partial success by employing certain strains of bacilli which were so slightly virulent that the animals spontaneously overcame the organisms. Krause has stated[16] that in the guinea pig the progression or regression of the lesion, when once established in the lymph node, bears a direct relation to the process in a peripheral focus. On the other hand, Martenstein and Amster[25] emphasized the fact that the skin and lymph nodes vary inversely in regard to the extent of tuberculous involvement. Krause and Willis[18] demonstrated that the spread of the Saranac H-37 strain of tubercle bacillus was greatly retarded in guinea pigs which had been previously sensitized with the Saranac R-1 variety of Koch's bacillus. Arima[2] concluded that by injecting a virulent strain of human tubercle bacillus into the parenchyma of the rabbit's testis a chronic form of the disease was obtained in enough animals to justify such a procedure being used where research on healing was the object. From a comparative study of experimental phthisis, Krause[17] considered that the dissimilarity in the location of certain lesions in guinea pigs as contrasted to rabbits pointed to the anatomic structure being an important determinant in tuberculosis. From the above excerpts it would seem that a more appropriate form of the disease might be experimentally produced, one in which a virulent strain of tubercle bacillus could be employed and yet the immunity of the animal be so increased by some agent that the localization of the organisms within the lymph nodes would bear a likeness to tuberculous adenitis of human beings. Then the results of therapy might be fairly evaluated, and the problem be placed on a less empirical basis than is now the case. But so long as the animals either die of a widespread disease, or are able unaided to throw it off, just so long will the proper appraisal of any form of nonspecific therapy, such as roentgen radiation, be very difficult.

Aside from the above, a second factor to consider is that the roentgen rays should be applied over such a part as to offset the difference in distance of the irradiated tissues from the source of the rays, for it is well known that the amount of radiant energy delivered to any one point varies inversely with the square of the distance from the point to the source of energy. Consequently, in a small beast, such as the guinea pig, the roentgen rays would be delivered to the internal parts of the body in a relatively much higher proportion to that received by the skin than would be the case in a large animal, such as man. If the site of the irradiation were over the abdomen, chest, or cranial cavity, there would almost certainly be a more profound general effect in the smaller creature. In order to exclude direct radiation from the viscera, one might utilize an area of the neck or the limb.

SUMMARY

In the *introduction* a partial review of the literature has been given in order to point out the interest that has been shown in the irradiation of infectious processes in general and of tuberculosis in particular. This relates to both in vitro and in vivo studies. In this connection it has been generally reported that the effect of the roentgen rays upon the tubercle bacillus itself (either outside or inside of the animal body) is

negligible, and this is especially true when one stays within the limits of therapeutic dosages.

The works of several authors have been reviewed showing that there is a general reaction on the part of the body when exposed to roentgen energy. The immediate importance of this to the present study is that numerous researchers have demonstrated that the tubercle bacillus migrates within a few hours from the site of inoculation; and, therefore, that any successful therapy must be intensely germicidal and be applied early or else it ought to evoke an adequate, general resistance on the part of the host.

Reports concerned with the actual results of roentgen therapy of experimental animal tuberculosis have been studied. In most of these (especially those appearing in late years) one may see that pessimism has justly reigned. A certain number of investigators have maintained that there was a reduction in the size of the regional lymph nodes together with less ulceration and abscess formation at the site of inoculation.

Papers from clinical observers have been cited to indicate that the results from the roentgen irradiation of human tuberculous cervical lymphadenitis have been encouraging.

The *purpose* of the present study was to transfer to animals the actual irradiation technique apparently so successfully employed by the Radiotherapy Department of the Cancer Institute, University of Louvain, Belgium.

One hundred and fifteen guinea pigs and 8 rabbits were *intracutaneously*, injected with different amounts of a very virulent and a scarcely virulent strain of tubercle bacillus; 69 of the guinea pigs and 4 of the rabbits were irradiated according to 4 different plans. The remaining animals were used for controls, i.e., inoculated but not irradiated.

The *results* were analyzed according to the amount of organisms given and the scheme of irradiation employed. Neither the rabbits injected with very virulent bacilli nor the guinea pigs inoculated with scarcely virulent bacilli ever exhibited any evidence of disease. In the other animals, as a rule, the larger the dose of tubercle bacillus, the shorter was the remaining duration of life. The formation of ulcers, but not that of abscesses, was likewise more frequently associated with the injection of the larger amounts of organisms. At autopsy the extent of visceral tuberculosis seemed to have no relation to the dosage.

The *effects of irradiation* were essentially negative except in the guinea pigs irradiated the day of inoculation according to Plan No. 4. These exhibited remarkable acceleration in the formation of ulcerations and abscesses at the site of injection, and in regional lymphadenomegaly, but this great increase in the local manifestations had no apparent effect upon the duration of life or the extent of ultimate visceral lesions. In the animals irradiated for eight weeks before the injection of tubercle bacilli (Plan No. 1) there seemed to be retardation of the local signs in the beginning but not in the later stages of the disease. The small number of animals in this group does not permit any emphasis to be placed upon the observations.

The *histologic findings* were slight increase in the connective tissue at the site of irradiation, the rarity of giant cells, the presence of both caseous and proliferative forms of tubercles, and the existence of a proliferative form of hepatic cirrhosis.

There has been appended a *theoretical discussion* indicating the lines along which future studies might possibly be pursued and pointing out some important defects in interpreting the results of investigations, including the present one.

CONCLUSIONS

1. Roentgen irradiation did not retard the progress of inoculated animal tuberculosis. That it exerted a deleterious influence was indicated but not proved.

2. The greater the dosage of organisms, the shorter was the remaining duration of

life, but at death the amount of visceral tuberculosis bore no relation to dosage.

3. The production of a chronic tuberculous cervical lymphadenitis in a small laboratory animal, similar to that spontaneously occurring in man, is necessary in order to place correctly the effects of certain therapeutic agents upon a comparative experimental basis.

I wish to state my appreciation to Dr. Samuel C. Harvey for his kindly, stimulating counsel and to Prof. J. Maisin (University of Louvain, Belgium) for suggesting the problem and placing at my disposal the necessary materials. Without the unstinted aid of Dr. Eugene Picard (Louvain) I should not have been able to complete the investigation, and to him I express my deep gratitude.

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HOW WE CAN MEET THE CANCER PROBLEM*

By HENRY J. ULLMANN, M.D.
Director, Department of Cancer Research, Santa Barbara Cottage Hospital
SANTA BARBARA, CALIFORNIA

IT IS only in a presidential address that one has an opportunity to preach to his colleagues; to express his thoughts and ideas rather than to tell of new discoveries, observations or procedures. The ideas here presented are not new but have either been forgotten or are unknown to a large part of the medical profession, especially to those not seeing or caring for large numbers of cancer sufferers. There is a hopelessness in regard to cancer shown by many physicians that is entirely unjustified, and in many instances this same attitude toward cancer is held by the laity. As a result, physicians are far too often advising their patients that there is no use in attempting treatment when, under adequate, modern methods, the life of this same patient might be prolonged in comfort or an actual cure be obtained.

Not many years ago to be told that one had consumption was equivalent to a death sentence and physicians were sending those with pulmonary tuberculosis, who could afford it, West, South, or anywhere, so that the responsibility for their care could be shifted to other shoulders. Then the public was aroused and societies were formed to fight the Great White Plague, but, fortunately, the problem was fairly well understood. The money was spent in educating the public in preventive measures, in providing sanatoriums where the sufferers could either be nursed back to health or their last days made comfortable. Hope was now offered to those suffering from that terrible mental anguish—hopelessness.

Only a small proportion, relative to the large sums spent on education, prevention and hospitalization, was spent in laboratory search for a cure. Search for a cure and better methods of treatment is still being made but never out of proportion to the efforts expended in producing actual cures by established methods of clinical care, in furnishing facilities for such care and for education in preventive measures.

Today, civilization must meet the challenge of the Great Red Plague, Cancer, as it was forced to meet that of the Great White Plague, Tuberculosis. The public is beginning to realize this and we must be prepared to act as leaders in the fight against this dread disease. Unfortunately, many of the profession are unaware of the problems involved and thus much effort and money are wasted while many victims are dying or suffering unnecessarily from cancer.

Man has sought for panaceas and specific cures from the earliest times and the public is eagerly awaiting the announcement of a specific treatment or cure for cancer. How unlikely it is that such a specific, applicable to all forms of cancer, will ever be found is only too painfully obvious to the intelligent student of cancer. But this does not apply to the development, by clinical and laboratory research, of successful methods of treatment even in the absence of a specific cure. The best example of the result of such research is insulin, a successful treatment but not a cure for diabetes. The percentage of actual cures among the commoner forms of cancer is being increased year by year as physicians become more and more skilled in the use of established and proved methods, and improvements in these methods are developed or discovered. It should be a matter of pride to the members of this Society that a large proportion of the reports showing such advances are made at its meetings.

Efforts directed toward meeting the cancer problem as a whole will accomplish far

* Presidential address delivered at the Sixteenth Annual Meeting, American Radium Society, Philadelphia, Penna., June 8–9, 1931.

more in saving life and relieving suffering than if devoted to clinical or laboratory research alone. Such research cannot accomplish much without adequate facilities for caring for and treating cancer patients. Many die unnecessarily from cancer because a lack of knowledge on their part results in a slowness to seek advice or to submit to treatment promptly when told that they have cancer. How often do we find patients refusing surgery or radiation because they have heard of some marvelous cure which will spare them the discomfort of such methods.

As there are only a few centers equipped with adequate facilities for treating all types of cancer, it is possible for only a small proportion of those needing such care to reach such an institution and therefore many cancer deaths result from lack of facilities, just as many deaths from tuberculosis resulted, not many years ago, from the lack of facilities for the care of its victims.

We can meet the cancer situation as it exists today by teaching the public and the profession that cancer is not necessarily hopeless as a large proportion can be cured by adequate modern methods, surgical and radiological, if treatment is begun in the early stages of the disease; that, therefore, those with cancer and those who suspect that they have cancer must seek advice, and submit to treatment early; that the percentage of cures in the earlier stages is increasing year by year with the exception of a small group of exceedingly malignant growths within which no cures have ever been reported.

We can teach the profession to recognize the early signs and symptoms of cancer and what to do for that particular cancer when found and to urge their patients to prevent cancer so far as possible by the prevention or eradication of foci of chronic irritation.

We must not only advise but urge those making donations to combat cancer to give their funds to meet the cancer problem, as a whole, not for any particular phase.

There are so much money and effort being wasted due to ignorance of the problems involved both within and without the medical profession that I shall take the liberty of quoting three paragraphs from a paper which I read before the Radiological Society at Los Angeles last December, as they express my idea of how this money and effort should be conserved and distributed.

The present tendency is, as soon as funds are provided, to erect and equip elaborate laboratory buildings, and the director of research is instructed to search for the cause of or a cure for cancer. No consideration is given those sufferers who might be relieved or cured if proper facilities for their care and treatment were provided. Each fund should be divided into three parts by the medical advisory board, and the relative size of these parts varied from time to time as the local situation demands. In this way the work will be balanced and the greatest benefit be obtained from any given amount of money available. For example, the laboratory research in an institution may reach an impasse or become abortive for lack of clinical material. The medical board may then divert sufficient funds to supply hospital accommodations until such time as the clinical research has caught up with the laboratory. Or again, the local situation may require a major portion of the budget to furnish facilities, such as radium, or to equip a clinic in order to obtain the greatest benefit for the cancer sufferers in that locality.

The physicians in the surrounding territory must be taught to recognize cancer and what to do when it is found. They must be taught that the treatment and diagnosis of cancer is a group problem and that team work with their colleagues is essential. They must be taught that the hopeless cancer sufferer must not be left to die with morphine as his only aid, but that the duty of a physician is to relieve suffering as well as to cure disease.

With institutions in the larger centers completely equipped and adequately staffed, each with laboratory facilities for research, diagnostic centers should be established in the smaller cities. Such a smaller center must be complete for its purpose and the staff must include a trained pathologist. Here patients may be referred for diagnosis and advice, for the staff must be in constant touch with the parent in-

stitution. Patients who can not be properly treated locally are referred to the large treatment center, where all facilities, including free care for indigents, are available. It is economically unsound to install expensive roentgen outfits and large supplies of radium in every city. These should be concentrated in the special centers and these centers distributed so far as possible that they may serve the surrounding population with the minimum of transportation problems. Close cooperation with the public health services should be maintained. These are particularly valuable in keeping check on patients after treatment.

May I, in closing, suggest that we leave this meeting of the Radium Society resolved, while well aware of the terrible seriousness of the cancer problem, to combat the feeling of hopelessness that is not infrequently found among uninformed physicians as well as the laity. If due to a series of failures we become pessimistic, let us ask ourselves if we had to have cancer and could choose the time, which would offer the most hope, fifteen or even ten years ago or today? Let us bring a feeling of optimism to our patients for, while the number of cancers is increasing, the percentage of cures is also increasing.

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A CLINICAL EVALUATION OF VARIOUS QUALITIES OF ROENTGEN AND RADIUM RAYS FOR THE TREATMENT OF ADVANCED CANCER*

By BERNARD P. WIDMANN, M.D.
Radiological Department, Philadelphia General Hospital
PHILADELPHIA, PENNSYLVANIA

THERE is no biological proof of a superiority of a particular wave-length for cancer therapy.

The quality of roentgen radiation obtained from 200 kv. and 0.5 mm. copper filtration admits of greater penetration at varying depths with less danger of damaging the skin than from 127 kv. and 6 mm. aluminum filtration.

The tissue absorption is less than with longer wave-length radiations, but clinical results belie these physical observations or justify the inference that secondary radiations are not particularly essential for adequate and efficient therapy or that there may be beneficial qualities of absorbed short wave-length radiations which our present physical equipment cannot estimate.

Up to the present time much has been accomplished in the radiation treatment of advanced cancer—standardization of equipment, estimation of skin tolerance for intensive treatments, systematizing fractional doses to the extent of skin saturation or tolerance and an evaluation of clinical responses on the basis of tumor grading according to its cellular differentiation.

In most instances, the sensitivity of a tumor is finally determined after radiation has been given. Occasionally complete regressions are seen before completion of a series of treatments. As these sensitive tumors are highly cellular, they are highly malignant, and irradiation should be continued at intervals of four to six weeks to obviate any possibility of recurrence.

The so-called palliative benefits from irradiation of most cases of advanced cancer have not been appreciably increased except insofar as there has been a more universal education concerning irradiation principles and a freer acceptance of these procedures, together with an acquisition of adequate facilities by many institutions throughout the world to carry on this work efficiently.

In an effort to further improve the results of irradiation of advanced cancer, it was thought advisable to make actual clinical observations on the effects of different qualities of radiations on a series of lip cancers, employing roentgen rays, 127 kv. with no filter, and with 2, 4 and 6 mm. aluminum filtration.

Eighteen cases of epithelioma of the lip were selected with involvements of apparently equal extent, all surgically operable and the types of cases usually successfully treated by electrodesiccation. Three cases in each group were given localized roentgen irradiation (127 kv. no filter; 2, 4 and 6 mm. aluminum). A total of 3 skin erythema doses for each quality of radiation was given at one sitting. The clinical cure in each of 12 cases was equally good.

Six cases of epithelioma of the lip were given surface applications of radium using filters of 0.5 mm. of silver (2 cases), 2 mm. of brass (2 cases), and 2 mm. of platinum (2 cases). The response in each instance was identical with the radium, using different filtrations and intensities of 3 S.E.D.

At the present time all advanced lip and intraoral cancers are treated with surface applications of gamma radium rays (filter, 2 mm. of platinum) with regressions comparable to those seen from gold seed implantations (radon).

Our clinical experience on the effect of short wave-length radium rays is based on its routine use in 69 cases of intraoral can-

* Read at the Thirty-first Annual Meeting, American Roentgen Ray Society, West Baden, Ind., Sept. 23–26, 1930.

cer. In divided doses of surface or contact applications, 4 to 6 erythema doses have been administered within four to six weeks, with reactions that are not appreciably greater than obtained with gold seed implantations.[1]

It is important to note that the quality of radium rays cannot be adequately interpreted on the basis of our present physical measurements with filtrations in excess of 2 mm. of brass. If 2 mm. of platinum is used, the metal density is 42 as compared to 17 which is the density of 2 mm. of brass. Our experience shows an erythema ratio of approximately 2.5 to 1.

Since short wave-length radiations are clinically as effectual as the longer wave-length radiations, and since greater total intensities can be obtained without skin damage, and with improved clinical results, measures were instituted to further increase the total quantity of radiation that might be delivered through a given skin area.

If the end-results of advanced cancer are to be improved with irradiation, some method of increasing the total quantity must be devised, and still preserve the physical integrity of the patient as well as the skin.

TECHNIQUE

Theoretically, 50 per cent of a skin erythema dose with a given quality of radiation added to 50 per cent of a skin erythema dose of another quality, should give an erythema equal to the intensity of 100 per cent S.E.D. of either one of these types of radiations. Quimby and Pack[2] have demonstrated experimentally an increased tolerance of the skin for combined qualities of radiation ("soft" and "hard").

In a series of 217 patients (Table 1) the skin tolerance was found to be decidedly greater when different qualities of short wave-length radium and roentgen radiations were employed.

The increased skin tolerance or saturation obtained during a period of about six weeks ranges between 230 and 280 per cent of a skin erythema dose through a single skin portal, depending on the qualities of the combined radiations. These observations were presented in a preliminary report by Widmann and Weatherwax,[3] and up to this time a total of 319 cases have completed treatments with combined high voltage roentgen rays (200 kv.) and gamma radium packs (2 mm. platinum) applied to the same skin area.

TABLE I

Filter and Quantity of Radiation		Per Cent S.E.D.	Saturation Point (6 wk.)	Number of Cases
0.5 mm. Cu		100	180	62
0.5 mm. Cu 65% S.E.D.	1 mm. Cu 65% S.E.D.	130	230	28
0.5 mm. Cu 70% S.E.D.	1.5 mm. Cu 70% S.E.D.	140	250	9
0.5 mm. Cu 70% S.E.D.	2.0 mm. Cu 75% S.E.D.	145	260	27
0.5 mm. Cu 70% S.E.D.	2 mm. Pl (radium) 85% S.E.D.	155	280	91
			Total	217

Roentgen-ray factors: 200 kv., 25 ma., 50 cm. distance, 10 x 15 cm. field, mechanical rectification, water-cooled tube, 820 r.

The skin tolerance or so-called "threshold erythema," is fairly uniform within a detectable 10± range. The gamma radium packs are filtered with fixed lead capsules, walls 3 mm. thick, and soldered to a copper plate 0.25 mm. thick. The radon is housed in glass fixed in silver tubes 0.5 mm. thick. The combined density of these metals is 40.5 as compared with 42 which is the density of 2 mm. of platinum. Twelve capsules are fixed to a copper plate, two rows of six capsules 2 cm. apart. The irradiated area is approximately 10×15 cm. A uniform distance is maintained with felt pads 4 cm. thick. With these factors an erythema of a deep red intensity is uniformly

obtained with a single dose of 15,000 mc.-hr. in about twenty-one days. This reaction persists for ten to fourteen days and fades to a deep bronzing or pigmentation of the skin, and has also been seen to terminate with desquamation about ten days later.

An average of 100–120 mc. of radium is used in a pack for forty-eight consecutive hours. The total intensity of radiation delivered in this time is approximately 5,000 mc.-hr. Routinely, four applications are made, two each week, with a resulting total intensity of 20,000 mc.-hr. to each skin area, with a total time of 192 hours, or approximately 125 per cent S.E.D.

If the neck is treated, four such radium packs are applied to each side. In pelvic cases, two areas are employed, one anteriorly and one posteriorly (total 8 packs). Each patient therefore receives a minimum total of radium irradiation amounting to 40,000 mc.-hr. As the intensities are small, the time required to complete this treatment is 384 hours divided into 8 periods of 48 hours each.

The extremities, chest and abdomen are similarly plotted.

In addition to the radium packs, high voltage roentgen rays (200 kv., 0.5 mm. copper) are also employed over the same areas treated with radium. The roentgen treatments are given on the day intervals between the pack treatments over the radium pack areas. In a pelvic case four fields of 20 per cent S.E.D. each are given; chest, abdomen, neck and extremity are likewise treated with multiple ports. A total of six treatments with 20 per cent S.E.D. is administered to each skin port. This four-field technique is carried out as recommended by Weatherwax and Widmann[4] so that the entire area is uniformly irradiated at one sitting.

Within a period of three to four weeks, a total of 120 per cent S.E.D. roentgen radiation, and 125 per cent S.E.D. gamma radium radiation is given to each area, making a total of 245 per cent S.E.D. When the physical condition of the patient permits, this treatment may be continued six to seven weeks (to saturation) and frequently a total skin intensity of 350 per cent S.E.D. may be obtained.

The depth intensity in an average pelvic case will range from 240 to 350 per cent S.E.D. from external radiation alone.

The intraoral cases receive 4 to 5 S.E.D. through the center of the tongue and neck when combined roentgen and radium radiation are used externally in conjunction with contact surface applications internally.

In 11 pelvic cases, four radium packs were used in addition to four fields of roentgen radiation. The total combined external radiation (radium pack, 125 per cent S.E.D.; roentgen rays, 120 per cent S.E.D.) amounts to 980 per cent S.E.D. and was found to cause an undue amount of prostration if the treatment time was crowded into four weeks. It is significant to point out that the skin reaction was not appreciably increased with the additional radium packs.

RESULTS

Of the 319 cases of advanced cancer observed for two years and embracing all anatomical types, 167, or 42 per cent, are living. The immediate palliative benefits were strikingly good. In no case with extensive gland involvement in the neck or pelvis is there any outlook of a clinical cure. Of 31 intraoral cases with metastasis (unilateral), regression was apparently complete in 9, but pain was not diminished. In 3 pelvic cases autopsy revealed regional metastasis, but complete disappearance of the extensive pelvic disease. The autopsy findings were similar in a late carcinoma of the bladder. Except for the healing of local ulcerations and regressions of skin nodules, postoperative recurrent breast cancer was not appreciably benefited over results obtained with the usual technique of roentgen irradiation alone. In no instance was carcinoma of the esophagus or stomach benefited.

Up to the present time it cannot be said on any statistical basis that combined qualities of radiation for advanced cancer

offer any material advance over the intensive use of one of these agents singly.

Many of the cases were not ideal from the standpoint of age, extent of involvement and good physique.

If an evaluation of combined qualities of short wave-length radiations were to be submitted on the basis of clinical impressions, then one could properly and justly voice an enthusiastic endorsement. Its merits at best are only relative and must yet remain in the category of "palliation." In an advanced case with good health and strength, the palliative benefits appeared to be more marked and more uniform than with intensive roentgen or radium pack treatment alone. This optimistic impression is conveyed with reservation, and is intended to imply observations on the immediate effects in selected late cases. Until a case can be observed for several years as clinically free of disease, no special superiority can be accredited to a particular technique.

Palliation is generally intended to imply any one of a score of proverbial epithets—cessation of bleeding or discharge, relief of pain, local or primary healing, improvement in health and strength and sometimes gain of weight, temporary or partial resumption of usual occupation or a mental buoyancy that gives the patient a "new lease" on life.

In the treatment of an advanced or hopelessly inoperable cancer, the accomplishment of any one or more of these improvements is indeed an achievement, even though it is so often only short-lived.

ADVANTAGES

Constitutional reactions were usually very slight. The increased physical tolerance for short wave-length radiation was evidenced by the ability of the great number of very advanced cases, and some very old and feeble cases, to stand intensive treatment over periods of three and four weeks.

An impoverished red blood cell count of 2,500,000 was never considered as a contraindication unless there was marked weakness or prostration. A drop of the white blood cells to 3,000 is always considered a contraindication to irradiation and is the signal to stop when it occurs during the course of treatment.

The skin tolerance is decidedly greater when two qualities of short-wave length radiations are combined. An experience with 319 cases treated with high voltage roentgen rays and gamma radium rays, covering an observation period of two years substantiates this statement.

The technique described above combines the advantages of the "fractional" doses with the prolonged and continuous (radium packs) irradiation over intermittent periods for three to four weeks. The condition of the skin at this time will generally permit continuing irradiation on the basis of saturation if the physical condition of the patient warrants.

The so-called low grade malignancies, usually very resistant to irradiation require oft-repeated treatments, sometimes over periods of one, two and three years, so that the increased tolerance of the skin for combined short wave-length rays is therefore particularly advantageous.

DISADVANTAGES

The technical procedures described above involve considerable expenditures to patient and hospital.

The radium resources—both private and institutional—for the most part, would be strained beyond capacity.

The procedure is economically almost prohibitive except in so-called radium centers, because a large supply of radium is essential if large numbers of patients are to be treated.

The substitution of radium packs for high voltage roentgen rays, alternating treatments with 0.5 and 1 mm. of copper and also 2 mm. of copper is recommended. This technique is now in progress at the Philadelphia General Hospital, and offers a solution of meeting the expense of combining short wave-length roentgen rays with gamma radium rays, but will not

overcome the advantages of the prolonged radium pack treatment over periods of forty-eight hours.

SUMMARY AND CONCLUSIONS

1. Equally good clinical results were obtained with long and short wave-length roentgen and radium rays in a series of epitheliomas of the lip.

2. Skin tolerance is greater for short wave-length radiations; there is more penetration but apparently less absorption.

3. Skin tolerance increased when different short wave-length radiations were combined (roentgen rays: 200 kv. and 0.5 mm. of copper; radium: filters of lead with densities equal to 2 mm. of platinum).

4. Radium packs with filtrations of lead and silver (3 mm. Pb and 0.5 mm. Ag approximately equal to the density of 2 mm. Pt) were employed for economical reasons, and represent densities approximately 2.5 times the usual 2 mm. of brass. The qualities of these radiations cannot be accurately interpreted with our present physical equipment.

5. The technique described incorporates the principle of Regaud—weak intensities for a long period of time (average 192 hours or 20,000 mc-hr. per field).

6. These combined qualities of radiation admit total intensities of 230 to 280 per cent S.E.D. through a given skin area by protracting treatment over a period of four to six weeks.

7. Improved clinical results justify the recommendation of combined short wave-length irradiation for advanced cancer.

8. Advantages and disadvantages of the method are discussed.

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CARCINOMA OF THE CERVIX

TECHNIQUE OF TREATMENT*

By WILLIAM P. HEALY, M.D., F.A.C.S.
NEW YORK CITY

THE principle underlying the plan of treatment of carcinoma of the cervix at the Memorial Hospital is to "cross-fire" with radium and roentgen rays the entire primary lesion and also the lymphatic drainage area through which the disease spreads from the primary focus.

This treatment is given in a relatively short time interval, using large quantities of radium. Sufficient filtration is used to give a fairly homogeneous gamma ray beam (0.5 mm. gold) but "heavy" filtration is not employed.

The complete treatment consists of a high voltage cycle to the entire pelvis, radium tandems in the cervical and uterine canals, vaginal applicators against the cervix, and, in some cases, interstitial irradiation by means of radon seeds buried in any part of the primary lesion which has not responded satisfactorily to the other treatments. An effort is made to utilize the heaviest doses of radium that can be applied to the diseased tissues without permanent or serious damage to the surrounding normal structures as well as avoiding, if possible, a too severe constitutional reaction.

In very early cases, with the lesion apparently limited to the vaginal cervix, radium is used first, followed by roentgen rays. However, in most cases it seems advantageous to begin the treatments with the roentgen-ray cycle in order to reduce the bulk of the lesion and diminish the inflammatory process before applying radium. This is, therefore, the routine procedure at present.

The actual cautery has been occasionally used to destroy a large cauliflower lesion of the cervix before applying radium or roentgen rays. In general, however, we believe it is preferable to irradiate such a lesion with high voltage roentgen rays, followed by the insertion of gold radon seeds, before using the cautery, as the danger of scattering viable cancer cells in the surgical manipulations would seem thereby to be greatly diminished.

Hysterectomy is done only for some persistent complication such as pyometra, or pus tubes, or rarely in an otherwise favorable case in which the lesion has not responded to radiation therapy.

The pelvic roentgen cycle consists of four treatments, two anterior and two posterior, fields about 12×15 cm., each receiving a dose of 700 to 800 r at a single sitting. Treatments may be given daily, or one or two days apart. Occasionally the treatments are given in divided doses, if condition of the patient seems to demand it.

The total dosage planned for the vaginal applicator is from 1,000 to 3,000 mc-hr., and that with the intrauterine tandem 2,000 mc-hr. in the cervical canal and 1,000 mc-hr. above or near the internal os.

Microscopic control of clinical diagnosis is very important, and a biopsy is done in every case.

An efficient follow-up system is extremely desirable, all patients are kept under close observation during the first six months, and are re-examined every two to four weeks. Thereafter they are seen at longer intervals, but an effort is made never to lose track of them.

THERAPEUTIC PROCEDURE

In general, the roentgen cycle is given first. For this the patient may be hospitalized or not, depending on her general condition. A treatment may be given on each of four consecutive days, the sequence being left anterior quadrant, left posterior,

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right posterior, right anterior. On the other hand, if the patient experiences much annoyance from the treatment such as gastrointestinal disturbance or general malaise, the treatments can be spaced farther apart.

For the vaginal and cervical treatments, the patient is always admitted to the hospital within ten days after the roentgen cycle has been completed. A vaginal applicator is applied against the cervix for a dose of 1,000–2,000 mc-hr. When feasible, this is followed by applications against the right lateral and left lateral vaginal fornices for 1,000 mc–hr. each, making a possible total dosage by this means of 3,000 to 4,000 mc-hr. to the cervix and the lymphatic drainage area on each side in the base of each broad ligament.

The vaginal applicators vary in shape and size. Each one contains 400 to 1,000 mc. of radon.

The vaginal treatment is followed in a [illegible] or two by the use of the tandem. The dose of 3,000 mc-hr. is given at one sitting, and usually takes not over twenty-four hours.

When these treatments are finished the primary lesion has been cross-fired from the cervical canal, the vaginal canal, and the external surface of the body. In cases favorable for complete regression, this sequence of applications finishes the essential steps in the treatment. In some cases, after the above series of treatments has been finished there will still be evidence of active disease in the cervix or vaginal fornix, and within four to six weeks after the first treatment is given, gold seeds, each containing 1.5 to 2 mc. of radon may be placed in the remaining lesion. (Sometimes it seems more desirable to give this additional treatment by means of a surface application with one of the vaginal applicators.) It seems less dangerous from the standpoint of spreading metastases to place the seeds at this time than at the time of the primary treatment. Also at this time they can be placed more accurately and with less danger of overdosage and damage to normal tissues, formation of fistula, etc., for by far the greater part of the original lesion will have disappeared.

We also feel that in many advanced cases the high voltage roentgen cycle can be repeated to advantage six or eight weeks after the first cycle.

When all of the above steps have been carried out, in a time interval varying from two to ten weeks according to the original condition of the lesion, no other routine treatment is contemplated. Further treatment will depend upon subsequent development of active disease. In favorable cases the entire cervical lesion disappears within eight weeks.

GENERAL CONSIDERATIONS

1. *Factors Influencing Treatment in Carcinoma of the Cervix.*

A. *Primary.*

The stage of disease has very little influence on the routine plan of treatment. The exceptions are the very advanced cases which are given only roentgen therapy. In these, in general, no radium is used unless an unusually favorable response is obtained to the roentgen rays. If this should happen, radium may be used, the method of application and dosage depending on the operator's judgment, but usually being restricted to vaginal treatments.

The *average* advanced case may require some interstitial irradiation with gold seeds after the primary treatment, whereas the early and borderline cases usually regress completely without the use of interstitial irradiation.

The histologic grade of the tumor does not influence the plan of treatment except in the more advanced cases.

In such cases treatment would be pushed much further in a Grade III radiosensitive type than in a Grade I radioresistant, clinically similar as far as the extent of the disease is concerned, since it is felt that the response would be much more satisfactory in the former.

Pyometra found at the time of the primary treatment is an unfortunate compli-

cation. It usually prevents the application of a full dose with intrauterine capsules, and moreover, in such a case the local tissue reaction and regression seem to be interfered with an retarded.

Cases with pyometra, if at all favorable clinically, that is, early or borderline, do better if hysterectomy is done after full radiation therapy has been carried out.

The presence of large myomata need not interfere with the routine plan of radiation therapy for carcinoma of the cervix. When this treatment has been fully carried out, the myomata may, if the occasion arises, be treated by myomectomy or supravaginal hysterectomy.

Bulky parametrial lesions resulting in swelling of the leg on the affected side are seldom benefited by irradiation, although pain may be temporarily alleviated.

In very obese patients, with a heavy pendulous abdomen, roentgen treatments cannot be used to advantage.

B. *Recurrent.*

Cases of carcinoma of the cervix recurrent in the vaginal vault after attempted surgical cure by hysterectomy should be treated by surface application of radium through the vagina, by interstitial radiation, and by high voltage roentgen rays. The roentgen cycle should be repeated once, in from four to six weeks. Where the recurrence after operation is extensive and involves not only the vaginal vault but the broad ligaments and the pelvic lymphatics, treatment as a rule should be limited to roentgen therapy.

Recurrence of disease after radiation therapy, if local and limited to the vaginal tube, may be treated by interstitial radiation or surface applicators but the prognosis is doubtful. Extensive local recurrence in or about the cervix after primary irradiation is not as a rule amenable to further radiation therapy, regardless of the histologic grade of the tumor.

C. *Palliative.*

In many cases, due to poor general condition of the patient, and the presence of a marked secondary anemia, palliation only can be attempted. In these cases, before the use of radiation it is necessary to restore the patient's strength. Transfusion is the best and quickest procedure for overcoming blood loss, and may be used to advantage at any time during the course of the treatment. Frequent warm antiseptic vaginal douches aid in reducing the local infection and thereby diminishing the toxic absorption.

Deep roentgen therapy has its greatest field of usefulness in such cases. The treatments may, if necessary, be given in divided doses while general medical measures are being carried out. In almost every instance such treatment will be followed by marked reduction in size of the ulcerated area, and in the amount of fungating infected cancer tissue. The bleeding and discharge diminish and the patient's strength gradually returns.

The roentgen cycle may be repeated to advantage in six or eight weeks, and in the interim, radium may be applied to the vaginal surface of the lesion. Occasionally a very radiosensitive lesion will respond so well to this treatment that it will be possible to go on with the full radium treatment. Such cases may thereby obtain two to five years' prolongation of life.

Intrapelvic glandular metastases do not seem to respond to external radiation therapy.

D. *Prophylactic.*

Prophylactic postoperative irradiation is indicated as routine treatment after hysterectomy for carcinoma of the cervix. This should be carried out by cross-firing the vaginal vault with radium by means of vaginal applicators and with high voltage roentgen rays, externally.

2. *Sequelae.*

Proctitis secondary to irradiation is usually of short duration and responds to rectal injections of small quantities of olive oil, a soft or liquid diet, opium and bismuth.

Bladder irritation is less frequently seen,

and may be controlled by urinary sedatives.

Late bladder ulcers appearing six months or a year, and even later, after radiation therapy, and not due to direct invasion of the bladder wall with cancer, are regarded as radiation or trophic ulcers resulting from fibrosis, endarteritis, and localized tissue damage due to interference with capillary circulation. Such an ulcer is a source of great distress from dysuria, frequency of urination, and bleeding. At times the bleeding is quite severe and has resulted in the death of the patient. In the majority of cases frequent instillation of solutions of argyrol results in a cure. In the more severe cases with profuse bleeding, suprapubic cystotomy should be done, the ulcer may then be cauterized with the actual cautery, after which, by maintaining suprapubic drainage for a time to keep the bladder contracted and at rest, a cure of the ulcer may be obtained.*

* For discussion see page 752.

RADIUM AS AN ADJUNCT TO SURGERY IN THE TREATMENT OF CARCINOMA OF THE FUNDUS OF THE UTERUS*

By HARRY H. BOWING, M.D., *and* ROBERT E. FRICKE, M.D.
Section on Therapeutic Radiology, The Mayo Clinic
ROCHESTER, MINNESOTA

CARCINOMA of the fundus of the uterus presents certain inherent characteristics, distinguishing it from carcinoma in other organs; it is found less common than carcinoma of the cervix, the ratio usually being reported as one to four or as low as one to eight.[10,30] Carcinoma of the fundus occurs at a later age.[10,11,13,15,16,28] The average age incidence is in the fifties; in most cases the patients have passed through the menopause. A small but definite percentage of the lesions are associated with uterine polypi and with chronic endometritis, and a much larger percentage are associated with myomas of the uterus (in the literature from 20 to 37 per cent of all cases),[10,25,32] the latter complication frequently masks the diagnosis. A characteristic of prognostic value is that the growth is confined by the uterine musculature for a long time and invasion and metastasis are relatively late.[16,20,31] Hence operation alone is more successful in carcinoma of the fundus of the uterus than in carcinoma of the stomach, rectum, or breast, for example.[32] However, metastasis to the vagina occurs with considerable frequency; Meigs[23] found it in 12 per cent of cases. The ovaries are involved in many cases, reports varying from 10 to 23 per cent.[10] Following operation most patients that succumb to the disease die within the first three years, 70 per cent from local recurrence.[32]

As is well known, metrorrhagia and brownish, watery and at times irritating vaginal discharge, usually with odor, are the cardinal signs. The pelvic examination may be negative, or the uterus may be found to be slightly enlarged. If the cervix is normal on inspection, carcinoma of the fundus must be suspected until it is disproved. The essentially diagnostic procedure is curettement; in some cases the Clark test will suffice.[7,25] The danger of curettage consists of transmission of malignant cells through the fallopian tubes, as stated by Clark and Norris, Faure and others, or possible perforation of a necrotic uterine wall. The value of curettage far outweighs its disadvantages. To obtain full value a skilled pathologist should examine the specimen, since the histologic picture in early cases may be quite confusing.[17,18,27]

Accepted modes of treatment are: operation alone, irradiation alone, or a combination of the two either as preoperative irradiation and operation or operation and irradiation afterward. The cooperation of surgeon and radiologist is most essential in this group of cases. Although radium is an invaluable palliative agent in advanced lesions, it also aids surgical methods by permitting a less radical operation. Many surgeons prefer vaginal hysterectomy and irradiation to extensive abdominal panhysterectomy.

In considering the present status of radiotherapy in carcinoma of the fundus of the uterus its limitations as well as its benefits must be evaluated. Early literature especially is pessimistic.[6,8,9,21,22,33,35] It is only of late years that certain writers[19,26] have become quite enthusiastic over future possibilities. One reason for pessimism is that the use of radium has been largely restricted to inoperable advanced growths and naturally the five-year results have been far from encouraging. However, many encouraging reports have appeared by careful workers.[1,2,3,4,5,7,13,14,24,34,36] Our satisfactory results occurred in early cases

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if contraindications to operation existed because of other complications such as obesity (19 cases in the operative and 37 in the nonoperative group) or poor general health of the patient. The main limitation of treatment with radium is that the required dosage, the exact placing, and the exact results cannot be accurately determined. As Kelly pointed out, we are working in an invisible field and have no method of determining the surface, extent, or depth of the lesion and the exact placing of applicators.

We have reviewed cases in which treatment was given with radium and roentgen rays at The Mayo Clinic from 1915 to 1928 inclusive. From the data obtained on examinations of the patient and those obtained at operation, the lesions were classified into four stages according to their anatomic limits as follows:

In the first stage* the growth was small with slight to moderate infiltration of the wall of the uterus, but strictly limited to the cavity of the fundus keeping within the level of the internal os. The uterus was movable.

In the second stage the uterus was usually increased in size. The lesion was comparatively large, infiltrating deeply the walls of the fundus and involving one or both cornua, with or without infiltration of the parametrium adjacent to the uterus. The uterus was movable.

In the third stage the uterus was small or large and was usually fixed. The following were characteristics: (1) definite infiltration of the parametrium on one or both sides extending to the wall of the pelvis with limited mobility of the uterus or infiltration of the parametrium on one side with fixation of the uterus; (2) more or less infiltration of a large part of the cervix or the presence of carcinoma protruding from the external os with or without involvement of the walls of the vagina and a mobile uterus; (3) isolated metastasis in the pelvic lymph nodes with a relatively small primary growth, and (4) isolated metastasis to the lower part of the vagina with or without involvement of the inguinal lymph nodes (all extensive lesions not placed in the fourth stage will be placed in the third stage).

In the fourth stage the uterus was usually enlarged, and fixed. The types constitute (1) carcinomatous perforation of the wall of the uterus with or without massive infiltration of the parametrium, extending to the wall of the pelvis; (2) carcinoma involving the retroperitoneal or lumbar lymph nodes and possibly the ovaries, fallopian tubes, intestines, bladder, rectum or labia; (3) infiltration of the entire uterus or of one or more walls of the vagina along its entire length with fixation of the primary growth; (4) remote metastasis; (5) involvement of the iliac and inguinal nodes, and (6) general carcinomatosis.

The age incidence in the 189 cases conforms closely to that recorded by other observers; it varied from twenty-nine to seventy-nine years; the average age was 57.5 years (Table 1). Computing according to stages, a gradual increase was noted in the average age from the first to the fourth stages, the oldest patients presenting the most advanced and hopeless lesions.

We were able to trace 172 (92.97 per cent) of the 189 cases and our conclusions were based on these cases.

In 87 cases some form of major surgical procedure was combined with irradiation. The average age in this group was 54.89 years. Total abdominal hysterectomy was performed in 61 cases (Table II) and vaginal hysterectomy in 10 cases. Except in a few cases the operations were performed at The Mayo Clinic. In 4 cases a tumor had been removed elsewhere, and in one case the cervix had been amputated. Definite pathologic data were obtained in all but 4 of the 87 cases. Adenocarcinoma of course was the predominating lesion; it was mixed with squamous-cell epithelioma in 3 cases, and squamous-cell epithelioma alone was found in one case. In 47 cases of adeno-

* In this early stage, Seides reported cures by curettage alone. Norris and Vogt reviewed 22 cases from the literature in which the entire lesion was removed by the curette.[25,29]

TABLE I

CARCINOMA OF UTERINE FUNDUS TREATED WITH RADIUM: AGE INCIDENCE

Age, years	Cases	Per cent	Stage			
			1*	2	3	4
20–29	1	0.52		1		
30–39	8	4.23		4	3	1
40–49	19	10.05	2	5	6	6
50–59	79	41.79	14	10	33	22
60–69	67	35.44	9	16	21	21
70–79	15	7.93		4	8	3
Total	189		25	40	71	53
Average age, years	57.5		56.28	56.77	57.63	58.14
Youngest, years	29		40	29	38	39
Oldest, years	79		69	79	75	76

* Stages of involvement in all tables are graded from 1 to 4, in which 1 indicates involvement confined to the uterine fundus and 4 extensive involvement of surrounding structures as well.

carcinoma malignancy was not graded; in the other cases, grade 2 predominated. Radium was employed in 11 cases before operation. It was used following operation at intervals of four to six weeks except in the cases in the fourth stage; in this group an average interval of fifteen weeks was allowed to pass in an effort to build up the patient's general health. In 2 cases of the fourth stage radium was abandoned because of the rapid advance of the disease. One of these patients died in the hospital. Usually one postoperative course of radium was given, but in the cases in the third and fourth stages, an average of two courses was given. If roentgen rays were applied following radium treatment the high voltage was used, instead of moderate voltage, as in the earlier years. In the 87 cases in which operation and radium were combined, 22 patients died within the first three years, 36 lived three years and 24 lived five years; 23 patients survived beyond the five-year limit. Of those that died the length of life after treatment varied from thirty-nine months in the first and third stages, to twelve months in the fourth stage.

In the cases of advanced inoperable lesions in which radium was used (Table III) the average age was 59.7 years, contrasting with 54.89 years in the cases in which operation was performed. As would be expected most of these lesions were in the third and fourth stages. In the few cases in which the lesions were in the first and second stages, the poor general health of the patient and various complications precluded surgical measures. Pathologic data were not obtained in 25 of the 102 cases, since the lesions were massive and clinically unmistakable, and since in earlier years biopsy was not so frequently employed. Twelve high-grade squamous-cell epitheliomas were found; among the graded adenocarcinomas, grade 2 again was in the majority.

Complete and adequate radium treat-

TABLE II

CARCINOMA OF THE UTERINE FUNDUS TREATED WITH RADIUM: PATIENTS WHO UNDERWENT OPERATION

Stage	Cases	Average age, years	Operation, cases						Average interval between operation and treatment by radium, weeks	Radium, treatment							Roentgen-ray treatment			Deaths in hospital	Results, patients						Cause of death			Dead
			Total abdominal hysterectomy	Subtotal abdominal hysterectomy	Vaginal hysterectomy	Cautery	Removal of tumor	Amputation of cervix		Complete	Limited	Prophylactic	Abandoned	Preoperative	Postoperative	Courses	Moderate voltage	High voltage	Abandoned		Untraced	Dead, lived less than 3 years	Lived 3 years	Lived 5 years	Lived more than 5 years	Living at last report	Carcinoma	Other causes	Cause unknown	Average life in months after treatment by radium
1	20	55.40	17	1	2				4	2	1	17		2	18	21	2	11	15			3	1	9	6	6	15	6			39.25
2	24	53.24	14	3	6	1			5.5	1	3	20		2	23	27	7	13	27			2	6	10	7	7	15	5	2		22.57
3	28	55.21	22	2	2	1	1		5.5	2	7	19		4	25	35	11	11	27	1		4	3	16	10	9	20		3	1	39.5
4	15	56.26	8	2		1	3	1	15	1	10	2	2	3	15	22	5	4	12	1			12	1	1	1			12	1	12.53
Total	87	54.89	61	8	10	3	4	1	7	6	21	58	2	11	81	105	25	39	81	1	9	22	36	24	23	50	22	4	2	22.32

TABLE III

CARCINOMA OF UTERINE FUNDUS TREATED WITH RADIUM: PATIENTS WHO DID NOT UNDERGO OPERATION

Stage	Cases	Average age, years	Radium, treatment						Roentgen-ray, treatment			Deaths in hospital	Results, patients						Cause of death			Dead
			Complete	Limited	Prophylactic	Abandoned	Courses		Moderate voltage	High voltage	Courses		Untraced	Dead, lived less than 3 years	Lived 3 years	Lived 5 years	Lived more than 5 years	Living at last report	Carcinoma	Other causes	Cause unknown	Average life in months after treatment
1	4	61.75	3	1			4		1	1	2		1	4	3	3	3	4	5		2	27.5
2	18	60.27	13	5			29		5	6	13		3	19	8	5	5	10	21	2	1	23.3
3	42	59.71	33	6	1	2	67		13	24	54			12	12	4	4	15	34	2	1	10.5
4	38	59.2	11	22		4	51		9	16	31	3		35	2			1				
Total	102	59.7	60	34	1	6	151		28	47	100	3	4	58	25	12	12	30	60	4	4	16.80

TABLE IV

CARCINOMA OF UTERINE FUNDUS: PATHOLOGICAL REPORT

Stage	Adenocarcinoma, cases					Squamous cell epithelioma, grade		Adeno-carcinoma and epi-thelioma, cases	Papillary adeno-carcinoma, cases	Inflam-matory reaction, cases	No data
	Grade				Not graded	Grade					
	1	2	3	4		3	4				
1	3	3	3		8			1	2	1	3
2	1	6		2	21		1		6	1	3
3		6	4	2	38	3	1	2	6	3	6
4	1	3	2	4	15	2	6	1	1	1	17
Total	5	18	9	8	82	5	8	4	15	6	29
Per cent	64.55 (122 cases)					6.87 (13 cases)		2.11	7.93	3.17	15.34

TABLE V

CARCINOMA OF THE UTERINE FUNDUS TREATED BY RADIUM: SUMMARY OF RESULTS IN TERMS OF DURATION OF LIFE

	Lived 3 years		Lived 5 years	
	Cases	Per cent	Cases	Per cent
Not subjected to operation Stage 1 and 2	11 (out of 16)	68.85	8 (out of 16)	50.00
Stage 3 and 4	13 (out of 64)	20.21	4 (out of 48)	8.33
Subjected to operation Stage 1 and 2	19 (out of 27)	70.37	13 (out of 18)	72.22
Stage 3 and 4	17 (out of 34)	50.00	10 (out of 27)	37.03

ment was given in only 60 of the 102 cases; in the remainder a limited course was given for palliative purposes. Six patients declined rapidly under treatment and further efforts were abandoned; 3 of these died in the hospital. Roentgen treatment was given in addition to radium treatment in most cases, one course on the average. Of the 102 patients, 58 died within a three-year period, 25 lived three years, and 12 survived at least five years. The average life after treatment varied from 27.5 months to 10.5 months in the fourth stage. It is significant that of the 4 patients with lesions in the first stage all are living at the last report and 3 of them are beyond the five-year period.

The pathologic data concerning 189 cases are tabulated in Table IV. In 29 (15.34 per cent) data were not obtained. In 6 cases (3.17 per cent) biopsy disclosed inflammatory tissue, although malignancy was unmistakable, clinically. Adenocarcinoma was found in 122 cases (64.55 per cent), papillary adenocarcinoma in 15 cases (7.93 per cent) squamous-cell epithelioma in 13

cases (6.87 per cent) and a mixture of epithelioma and adenocarcinoma in 4 cases (2.11 per cent).

Results at the end of three years and five years have been calculated in the traced cases, grouping them in the first and second stages, and in the third and fourth stages (Table v). These were computed by omitting from consideration those in which treatment was too recent for the requisite period of survival. In the first and second stages there were 19 of 27 cases (70.37 per cent) in the three-year survival period and 13 of 18 cases (72.22 per cent) in the five-year period. In the third and fourth stages 17 cases (50 per cent) were in the three-year period, and 10 cases (37.03 per cent) were in the five-year period. In the first and second stages in which irradiation only was given, 68.75 per cent were in the three-year period and 50 per cent were in the five-year period. In the third and fourth stages 20.21 per cent of cases were in the three-year period and 8.33 per cent were in the five-year period.

SUMMARY AND CONCLUSIONS

One hundred and eighty-nine cases of carcinoma of the fundus of the uterus were referred for treatment to the department of therapeutic radiology during the years 1916 to 1929 inclusive. The mortality was 2.11 per cent. One hundred and seventy-two (92.97 per cent) of the patients have been traced. Eighty (46.51 per cent) of these were alive at last report; 92 (53.48 per cent) have died. Four of the 92 who were operated on, and 4 who were not, died of causes other than carcinoma, such as senility, myocarditis and bronchopneumonia. Thirty-six (20.93 per cent) of the patients had lived for five years, and 61 (35.46 per cent) had lived for three years.

Of the 189 patients, 87 were treated by operation and irradiation, and 102 were treated by irradiation only. Results were naturally better in the earlier and more favorable operable series; 31.16 per cent of patients survived for the five-year period and 46.75 per cent for the three-year period. The percentages in the nonoperative series were 12.63 and 26.31, respectively.

Computing the three-year results up to 1929 and the five-year results up to 1927 we find a much higher percentage of satisfactory results. Operation and irradiation yielded 72.22 per cent of five-year cures in the first and second stages and 37.03 per cent in the third and fourth stages; in the nonoperative group, irradiation alone gave 50 per cent five-year cures in the first and second stages, and 8.33 per cent in the third and fourth stages.

Cases of carcinoma of the fundus referred to the radiologist for treatment fall into two groups. The larger group is made up of widespread lesions which preclude any possible hope from operative procedures and a few cases of small localized carcinomas but with complicating factors in which the general health of the patient contraindicates operation. The smaller group is made up of patients in better general health and with smaller lesions, in which surgeon and radiologist cooperate in attempting cure. As would be expected, much better results are obtained in the latter group. Although the large number of massive lesions treated decreases the number of five-year cures from the standpoint of irradiation, the late results in a few favorable cases in which irradiation alone was used compare favorably with the results when operation alone was the treatment; this forecasts the probable future development of irradiation in carcinoma of the fundus of the uterus.

Irradiation is an invaluable adjunct to operative procedures in the treatment of carcinoma of the fundus of the uterus. At the present time and with the accepted modes of treatment, surgery is the treatment of choice if the size of the growth and the patient's general health keep the surgical risk within normal limits. Operation discloses the true extent of the disease, whereas radium is handicapped because the application must be made in an invisible and indefinite field. That radium and

roentgen rays possess definite value in treatment is shown by the good end-results in the small number of localized lesions in the first and second stages in which complications precluded surgery. Irradiation alone yields high returns in palliation but poor remote results, mainly because the majority of lesions are too advanced to permit adequate treatment. Irradiation can be applied with relative safety, even for massive hopeless lesions. The four patients who died (2.11 per cent) all had lesions of the fourth stage; this percentage compares favorably with the surgical mortality rate of 5.4 per cent in the series of 333 cases reported by Stacy from the Clinic.

Hence we conclude that irradiation accomplishes commendable results. The surgeon is relieved of accepting high operative risks and may perform less radical operations by combining his work with carefully applied radiotherapeutic measures.*

* For discussion see page 752.

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RADIATION THERAPY OF CANCER OF THE CERVIX AT BELLEVUE HOSPITAL*

By IRA I. KAPLAN, B.S., M.D.
Director, Division of Cancer, Department of Hospitals;
Attending Radiation Therapist, Bellevue Hospital
NEW YORK CITY

BECAUSE of the marked prevalence of cancer of the cervix among women all over the world and the high mortality resulting from radical surgical procedures, irradiation has become in recent years the therapy of choice for this condition. Indeed so generally has this procedure come to be accepted as the proper one in the treatment of cancer of the cervix, that in 1929 the League of Nations appointed a Committee representing the three great medical centers in Europe to inquire into this subject and report on a plan for the further guidance of those desiring to take care of this disease in a standard manner. The conclusion arrived at by this Committee is that irradiation, properly carried out, is the treatment of choice for cancer of the cervix.

At Bellevue Hospital, New York City, irradiation has, since 1924, replaced all operative procedures in the treatment of this condition, and since 1929 this method has been the standard therapy for cancer of the cervix in the cancer units under the jurisdiction of the Department of Hospitals of the City of New York.

The radiation treatment adopted by the Division of Cancer and employed by the Radiation Department of Bellevue Hospital is a modified form of the Regaud plan described by Deschambre in 1923, as that in use at the Curie Institute, Paris, and was described by me in 1926, at the meeting of the Radiological Society of North America in Milwaukee. With a few later modifications this same method is in use today. Although Heyman has proposed the method of repeated radium applications to the cervix at set intervals, we have found that we obtain better results by following the Regaud technique of making the whole attack on the lesion at one time, applying small doses of radium, heavily filtered, over a long period of time.

For the treatment of the lymphatic areas draining the local cervix lesion, irradiation by high voltage roentgen rays has proved adequate and equally efficacious as pelvic irradiation with the radium pack. During the past year in treating the local condition, we have increased the amount of radiation delivered to the cervical and uterine canal because we noted that recurrences seemed to spring from the mucosa of this tissue even after giving intensive radium dosage to the vaginal portion of the cervix. In addition a second course of roentgen therapy is given to patients showing parametrial involvement eight to ten weeks after radium treatment.

In caring for those cases where excessive loss of blood had occurred we found transfusions to be of marked help in carrying these patients through, and this procedure was followed in all cases where the financial condition of the patient permitted. In all cases which showed any evidence of dehydration, a saline clysis was given when the radium application was made to the cervix lesion. Where the cervix mass was large, ulcerating and cauliflower in form, a large part of this excessive tumor growth was first removed surgically, usually by the endotherm, before radium therapy was applied.

Unfortunately, no case received was in such a condition as to be surgically considered, and all cases herewith reported had involvement of the surrounding tissues in addition to the local lesion. The economic status of patients in a free clinic such as ours, controls the stage at which our cases

* From the Gynecological Service, Dr. Fred C. Holden, Director, and the Radiation Therapy Division, Bellevue Hospital, New York City. Read at the Sixteenth Annual Meeting, American Radium Society, Philadelphia, Pa., June 8–9, 1931.

come for relief, which is in accord with the view of Freedman, who states that the incidence of cancer of the cervix is higher in the poorer classes than in the well-to-do. The early initial symptoms given immediate attention by the well-to-do are either overlooked or disregarded by the poor women who have to work constantly to maintain existence for themselves and their families, and therefore it is that only cases with extension beyond the site of the initial lesion are seen in the clinic.

For the same reason too, observation and care following treatment are very difficult to regulate. Not always is it possible for these poor women to return when they should for the follow-up observation that is important in order that possible recurrences may be cared for in an early stage. Furthermore, the poverty of these patients effectively bars more than a short convalescent period, while extra nourishment for building up the body strength against further inroads of the carcinoma tendency to cachexia is seldom possible.

Because Bellevue Hospital is a free, municipal institution accepting on an equal basis all types of patients regardless of race, creed or color, we have been afforded the opportunities of making some interesting observations. Thus, on account of New York's very numerous colored population, it is but natural that a large number of negro women suffering from cancer of the cervix should apply for care to the largest municipal hospital, and of the 138 cases reported herewith, 21 women, or approximately 16 per cent, were colored. Of the 117 white patients, 46 were native born Americans, and only 6 of the total number of cases treated, or about 4 per cent, were Jewish. While as a whole the number of Jewish patients coming to Bellevue Hospital is still small, the last figure mentioned bears out the findings reported by Hoffman in his study of the mortality of cancer throughout the world in 1915, and by Vineberg, in his study of the statistics of a very large Jewish hospital in 1919, and recently by Freedman, in his study of the incidences of cancer of the cervix in his report in 1931.

Not all cases of malignant involvement of the cervix were treated by this department, although all cases numbering 234 were referred to the radiation therapist for disposition. After examination, the cases were classified according to Schmitz' grouping, and 96 in Group 4 were transferred to the special hospital for custodial care only, where 70 died within a short period of time. Inasmuch as Bellevue Hospital is primarily for acute cases we deemed the above procedure proper and justified; in fact we have felt, with many others, that irradiation in such cases is detrimental and only increases the misery of the patient. Most of the patients treated by us belonged either to Group 2 or Group 3, and only 4 to Group 5. We have never received a Group 1 case for treatment.

In our experience we have not been able to use the pathological findings in our cases to prognosticate the course of the disease, but they have helped in planning the dosage of radium to be used in any given case. All cases except two were biopsied by us and classified pathologically, according to the histological findings. In our cases the plexiform type of epithelioma was most numerous, and while as Healy has shown, very radiosensitive, it was also most destructive. In 7 cases the histological picture showed a malignancy which was difficult to classify into one of the standard groupings. One, in particular, showed adenocarcinoma, squamous cell and plexiform epithelioma in one and the same section biopsied from the cervix. The pathological findings were as follows:

Plexiform	88
Squamous cell	31
Basal cell	1
Adenocarcinoma	9
Undifferentiated	7
Biopsy elsewhere	2

Whether or not marriage plays an important part in the incidence of malignancy of the cervix is still a moot question. In our series it would appear that marriage did increase the incidence of cancer. Less than

3 per cent of our cases were unmarried. As to whether the fact that a woman has borne children, affects the incidence of cancer of the cervix, a study of our cases inclines us to agree with Farrar, that injury of the cervix due to child-birth increases the occurrence of cancer. Only 9 cases definitely had no children, while 42 had more than 5 children.

The report as to marital state and number of children is as follows:

138 Cases
131 Married
3 Single
4 Unknown

Child-birth	
9	None
21	1 child each
18	2 children each
16	3 children each
10	4 children each
11	5 children each
42 over	5 children each
11 unknown.	

Unless specially indicated, operation was not performed in any case referred to us for irradiation. In only 10 cases was amputation of the cervix done to facilitate the application of the radium. This method of procedure is carried out also in Graves Clinic in Boston, as described by Bartlett and Smith. It is done to relieve the body of an excessive amount of malignant tissue and thereby aid the effectiveness of the radium therapy. In 4 cases the patients were referred to us following supracervical hysterectomy, performed elsewhere and with recurrences locally. The operative grouping was as follows:

No operation	124
Cervix amputation	10
Supracervical hysterectomy	4

In the matter of cancer of the cervix, we are inclined to revise our ideas as to the effect of age incidence and no longer regard cancer as a disease of old age, since 40 per cent of our cases were below forty years of age. The youngest patient was twenty and 3 were over sixty-five years old. The age incidence was as follows:

Age	Cases
20–30	16
31–40	40
41–50	50
51–65	26
66 and over	3
Unknown	3

The number of patients accepted for irradiation according to year when admitted to the service is as follows:

Year	Cases
1925	15
1926	14
1927	25
1928	25
1929	24
1930	35

It is a source of gratification to us that we have reason to feel that with our treatment all cases had their intense symptoms ameliorated, and that real benefit was afforded to practically all of them. In no case treated by our method was a rectovaginal or vesicovaginal fistula produced. Most of the patients who died succumbed to pelvic extension and metastasis, and nearly all cases showed local healing following the radium application. One hundred and twelve patients are alive and there are 26 known dead; of the living 15 are alive more than three years. The following table shows the classification of patients still living after radiation treatment:

	Cases
1 year	61
1–2 years	23
2–3 years	13
3–4 years	10
4–5 years	4
over 5 years	1

The time was calculated from the date of treatment to the date of the last recorded visit to the clinic, but as in many instances this was several years ago, some of those patients undoubtedly must have lived beyond the period recorded on our charts. As previously stated the class of patients seen at this large charity hospital does not lend itself to accurate follow-up observations.

Of the known dead 6 are of the 1925 group of 15 cases and the others as follows:

14 cases –1926.....5 dead
25 cases –1927.....4 dead
25 cases –1928.....5 dead
24 cases –1929.....5 dead
35 cases –1930.....1 dead

Occasionally complications more or less severe followed irradiation, the most frequent being a localized pelvic infection. In 2 such cases incision and drainage of the posterior cul-de-sac cleared up the condition. A latent gonorrheal involvement of the adnexa may be lighted up and give trouble. In such cases removal of the radium followed by expectant treatment readily clears up the pelvic condition, and radium is again applied to the local malignant lesion when the infection subsides. One death followed traumatic perforation of the uterus.

SUMMARY

1. In our opinion, carcinoma of the cervix is best treated by irradiation.

2. At Bellevue Hospital irradiation has replaced operation for this condition.

3. The method employed is that first established by Regaud and modified to its present form.

4. Treatment is by roentgen rays and radium.

5. Complications are treated in the normal gynecological manner for pelvic infections.

6. Statistics are given of 138 cases treated by the Radiation Department of Bellevue Hospital in the years 1925–1930.

For the preparation of the statistical data for this paper the writer expresses his thanks to Dr. Benjamin Feuerstein, resident in Radiation Therapy at Bellevue Hospital.*

*For discussion see page 752.

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A TUMOR-INHIBITING SUBSTANCE IN THE ROUS CHICKEN SARCOMA*

By M. J. SITTENFIELD, M.D.
NEW YORK CITY

THE fact that a filtrable substance obtained from the Rous chicken sarcoma gives rise histologically and biologically to the identical selfsame type of tumor has made this ultramicroscopic agent a subject of intensive research. As a result of this, experimental studies during the past few years have actually revealed important findings, particularly those of the physical and biological behavior of the tumor-producing substance.

In experiments which we [1,2,3] published recently, we reported that the tumor-producing agent of a filtrate could be maintained in glycerine for sixty days or longer without loss of potency. The chemical reaction of the filtrate is neutral, or like that of blood or other body fluids or tissues. This reaction of the blood varies but little under normal and even under pathological conditions. The blood maintains the same neutral reaction around pH 7.2 to 7.4, regardless of the intake of excess acids or alkalis. In other words, the blood itself is at all times a perfectly buffered solution. There are times when the alkali reserve may be nearly depleted, yet the hydrogen ion concentration of the blood and body fluids remains the same. These introductory remarks have an important bearing upon the work about to be described.

Sugiura and Benedict[4] reported in 1925 that fragments of mammalian tumors and emulsions of the chicken sarcoma when immersed for twenty-four hours in solutions of varying hydrogen ion concentrations from pH 3.8 to pH 11 or 12 sustain no loss of tumor-producing activity. Lewis and Michaelis[5] described experiments in which various buffer solutions were used, and concluded that the nature of the buffer solution within the same range of hydrogen ion concentration did not influence the infectivity of the tumor emulsions or extracts. So too, Murphy and others,[6] two years ago, stated that he was able to precipitate the filtrate with a weak acid, and to dissolve it in an alkaline solution without the slightest change in the virulence of the tumor-producing principle.

In our early experiments attempting to adsorb the tumor-producing agent with aluminum hydroxide and other adsorbents, we found by changing the chemical reaction of the filtrate, normally pH 7.2 to the acid side or pH 4, that the active agent was carried down with the precipitate. At this reaction of pH 4, the precipitate is only partially infective, that is, tumors result in about 30 to 50 per cent, while the ordinary filtrate gives rise to tumors in practically 100 per cent with our technique in doses of 0.5 c.c., which is practically twice the tumor-producing dose. From past experience we know that our filtrate produces tumors with 0.25 c.c., and at times even with 0.1 c.c.

While the tumor-producing agent at pH 4 gives rise to tumors in 50 per cent of the inoculations of the precipitate, the supernatant fluid becomes completely inert or non-infective, indicating that the substance which has to do with tumor formation is entirely removed from the supernatant fluid. To prove that the active agent is not chemically impaired by the acid reaction at pH 4, we shifted the pH of the precipitate to the alkaline side, or to pH 8, and upon bringing it up to the original volume, found that the causative agent at this reaction is completely set free, and to our amazement, it proved to be twice as infectious as the original filtrate. The shifting of the hydrogen ion concentration of the filtrate to the desired alkaline range can be repeated many times, and always with the same phe-

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nomena, that is, the supernatant fluid becomes entirely inactive, while the precipitate is only partly potent. The extraction of the precipitate at pH 8, however, intensifies the tumor-producing activity.

In explaining the increased tumor-producing activity, it naturally brought up the question as to whether the filtrable agent may possibly be in combination with a restraining or inhibitory mechanism, which becomes dissociated when the active agent is carried down with the precipitate. To put this in another form, once the tumor-producing agent was separated from the inhibitory influence, it had full play to exert its unrestrained activity so that now 0.1 c.c. or less than one-half the normal dose caused tumors. To test or demonstrate the presence of an inhibiting substance in the supernatant fluid, we mixed the filtrate with the supernatant fluid in the proportion of twice the tumor-producing dose, or 0.5 c.c. of the filtrate with 2 c.c. of supernatant fluid which had been concentrated in vacuo to one-half its original volume, and found that in 75 per cent of the 80 chickens inoculated, no tumor growth resulted. This means that the inhibitory substance in the supernatant fluid had neutralized the infective portion to such an extent that 59 out of the 80 chicks were protected. On the other hand, in the 21 chicks which did develop tumors, the tumors grew rather slowly, appeared at a much delayed period, and in a few instances receded after a nodule had formed.

That this failure to obtain tumors from a definite mixture of filtrate and supernatant fluid was not due to a chemical destruction was further proved by other experiments which proved that the tumor-producing principle could be recovered or released from a neutralized mixture so that it produces tumors from the same dose as that of the original filtrate.

The finding of an inhibitory mechanism in the tumor itself caused us to suspect the presence of a similar mechanism in the blood and body tissues. For this reason we tested the serum of normal chickens and that of tumor-bearing chicks. It was found that the inhibitory effect of normal serum was practically the same as that of the supernatant fluid of the tumor filtrate, that is, from 2 to 4 c.c., of serum neutralizes 0.5 c.c., of a 10 per cent filtrate, or double the tumor-producing dose.

In contrast to this, the serum of a tumor-bearing fowl in the late stages of the disease did not show any inhibiting effect, because tumor developed regularly indicating that inhibitory influence played no part. Whether this inhibitory effect is definitely specific or not, has up to the present not been fully worked out, as we have had no opportunity to test it against other filtrable tumors.

Chemical analysis of the inhibitory substance shows it to be bound up with the globulin fraction of the protein. In our experimental work, we were not able to obtain protection from the albumin portion in a single instance.

From what has been said, it seems clear, according to our present state of knowledge that the filtrable agent in the precipitate suffers partial loss of infectivity when the reaction of the filtrate is adjusted to the acid range. At this range, the supernatant fluid is entirely deprived of tumor-producing activity even in doses of 2 to 4 c.c., whereas the filtrate gives rise to tumors in doses of 0.25 c.c. Moreover, that this partial loss of infectivity of the tumor-producing agent in the precipitate is not due to chemical destruction is proved by the fact that it can be completely recovered by shifting the acid reaction to an alkaline one. At this reaction not alone does the tumor-producing agent exert its normal virulence but more than that, its activity is definitely enhanced because smaller doses will now give rise to tumor formation, and besides the nodules grow more rapidly and appear at a much earlier period.

This phenomenon of increased tumor-producing power rules out the possibility of the presence of cell fragments as a factor for tumor production. Every now and then someone denies a filtrable agent, and as-

cribes the tumors as a result of cell fragments which may have passed through the filter. In view of what has been said, it would be quite inconceivable that cell fragments in the filtrate could incite increased infectivity since it has been proved that the inhibitory substance has no effect against tumor cells or tumor fragments.

The neutralizing effect just described exerts its action upon the causative agent when it is no longer contained within the cells. In this respect it resembles the action of neutralizing bodies in virus diseases.

Murphy[7] and his coworkers, experimenting with desiccated tumor tissue, have since confirmed the presence of an inhibitory principle in the Rous chicken sarcoma.

It is obvious that the inhibiting substance is present only in the supernatant fluid from the filtrate when it is first precipitated at pH 4. This protective mechanism seems part and parcel of the tumor itself, because when it is dissociated and left behind in the supernatant fluid of the first precipitate it can no longer be demonstrated in subsequent precipitations. Supernatant fluid from the second, third or fourth precipitations at pH 4 in our experiments proved to possess no inhibitory effect.

On the other hand, the active agent of the tumor is not lost by successive precipitations, and dilutions, though the volume of the precipitate in the third, and fourth precipitations shrinks to 1/30 the bulk of the original first precipitate; yet when this tiny precipitate is suspended in a buffer solution and is brought back to its original volume, it is just as infective as the original filtrate. In other words, this would show that it is possible to concentrate and purify the tumor-producing agent in the filtrate and, moreover, by means of this concentration and purification to arrive at more precise knowledge concerning its physical and chemical or biological nature, also to obtain vital information of neutralizing and possible immunizing against the Rous chicken sarcoma.

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DISCUSSION ON PAPERS BY HEALY, BOWING AND FRICKE, KAPLAN, AND SITTENFIELD

DR. H. J. BAGG, New York City. Small pieces of mammalian tumors retain their ability to grow after being placed in solution of nearly pH 4 to pH 12. Dr. Sugiura of our laboratory was the first to study this problem. It is interesting to note that Dr. Sittenfield now examines the behavior of the tumor-producing agent in the cell-free filtrate of a chicken sarcoma, when subjected to varying hydrogen ion concentrations. At pH 4 acidity with the active agent carried down in the precipitate and the supernatant fluid inactive, we hear that the precipitate suspended in an alkaline buffer solution of pH 8 now shows an *increased infectivity*. Was the inhibiting substance in the supernatant fluid? This paper furnishes the laboratory test and answer to the question.

It is only by such careful weighing of evidence, by formulating a tentative hypothesis, and by performing the final experimental test that light can be thrown on this baffling problem of growth stimulation. May I congratulate Dr. Sittenfield on his excellent paper. I have only one suggestion to make; in order to sub-

stantiate the conclusion of the presence of *increased* infectivity of the tumor, after the methods used in this investigation, a large number of observations must be made, the degree of variation in normal growth established, and the significance of the results established by statistical means.

Dr. Charles C. Norris, Philadelphia. My colleague, Dr. Keene, at the Hospital of the University of Pennsylvania working in the same clinic with me, is now correlating the results in carcinoma of the cervix and for that reason I will confine my remarks to carcinoma of the fundus.

In general, I am in accord with Drs. Bowing and Fricke regarding the treatment of patients suffering from this tumor. Carcinoma of the fundus is a more malignant form of cancer and yields less satisfactory results from operative treatment than is often supposed. Until we conducted a follow-up of our cases a few years ago I believed that we were curing 60 to 75 per cent of them by operation. As a matter of fact, we found that we had 34.8 per cent of our total series alive and apparently without recurrences after three years. Like all cancer statistics, the more carefully the end-results are analyzed, the less satisfactory they are. Thus, Wilson secured 24 per cent of cures, and the recent reports from the Crile Clinic show less than 15 per cent. I prefer operation for early cases, but have no hesitancy about employing radium in the more advanced ones, or in those in which a radical operation is contraindicated. Many cases fall in the latter groups. I have been able to trace 21 three year cases, treated by irradiation alone, and of these, 8 patients are alive and apparently without recurrence. This compares favorably with our operative results, for whereas we cure about 66 per cent of the early cases by operation, the results in our series are far less satisfactory. We are all interested in getting the best results for our patients. Carcinoma of the cervix is a different proposition than carcinoma of the fundus. All local growths of the fundus can be cured by operation, except those few patients who are lost through operative mortality. It is questionable if intrauterine irradiation can do more than this. Carcinoma of the fundus is generally less embryonal than cervical and, therefore, rather heavier doses of radium are required. When irradiation is selected better results, I think, are secured by repeating the treatment two or three times, giving a total of not less than 4,000 to 6,000 milligram-hours. For palliative results in advanced cases smaller doses are often indicated.

Among 92 cases treated by radical operation there was one postoperative fatality, from peritonitis. Postoperative irradiation may be valuable.

I believe that when diagnostic curettage is performed in a case suspected of being one of carcinoma of the fundus, intrauterine radium irradiation should be employed at the same time. Most of these patients are at the menopausal age and this procedure tends to lessen the danger of dissemination either by the lymphatics, blood stream or transtubal routes, and increases the percentage of ultimate cures if we later resort to hysterectomy, and is curative if the condition proves to be a functional hemorrhage or other benign condition.

However, early diagnosis has a more important bearing upon the end-results than the type of treatment. Diagnostic curettage is the most certain method of arriving at a diagnosis and is especially valuable in the early case in which recognition is the most difficult.

In this connection I would like to mention the diagnostic test suggested by the late John G. Clark. This consists in the passage of a sterile sound under aseptic conditions to the fundus of the uterus, and the gentle manipulation of the point of the instrument over the surface of the uterine cavity. If a friable, vascular growth such as is produced by carcinoma is present a trickle of blood will follow. This test is not a substitute for diagnostic curettage, but is often valuable and may be employed as an office procedure. It is simple, requires no special pathologic knowledge or armamentaria, and when negative generally excludes carcinoma at once.

Dr. Henry Schmitz, Chicago. The work of Dr. Sittenfield is very valuable. It has been known for a long time that a patient suffering from a carcinoma has lost the carcinolytic property in his own serum which is present in humans who do not have cancer. In 1920 Koritschoner and Morgenstern investigated the serum of patients who had carcinoma and were operated upon and in each and every instance the carcinolytic property returned and remained present until they developed a recurrence. We decided to verify this work and in 1923 we examined the serum of 18 patients,

using the Freud-Kaminer method. The patients were all tested before they had radiation therapy, giving a negative carcinolysis, and after radiation therapy and as soon as their clinical cure was complete they had all regained their carcinolytic property and retained it until a recurrence would occur, i.e., if carcinoma did recur and not otherwise. Radiation therefore may be as effectual to eradicate cancer as surgery.

When we listen to the technique used by the essayists, and consider the differences in the application, and the varying amounts of radium used, we see that if we study carcinoma statistics from clinics using radiation therapy we should always study the technique of application of radiation dose. Curiously, the five-year good end-results seem definitely to be about 25 per cent. Wide differences are found in those clinics that must treat a large percentage of advanced cases. In Chicago the early Group 1 and 2 cases number about one-fourth of the total number treated, but represent one-half of the total good end-results.

There should be some way of standardizing the technique of radiation treatment. It is a fair hopefulness to individualize the treatment. Yet surgical radical treatment of cancer uses an absolutely standardized technique of wide dissection, regardless of the histological malignancy index or the clinical grouping. If the lethal carcinoma radiation tissue dose for uterine tumors should be 5 S.E.D. then a method should be developed by which that dose may be homogeneously distributed throughout the true pelvis.

In Chicago the combination of roentgen rays and radium has always been used. If there is anything proving the advantage of this method then the good end-results might be perused. From 1914 to 1919 the percentage of our five-year results, treated through six to ten small skin areas, with a voltage that was unstable due to the type of transformers, was 14.5. When we changed to the large field our results went up to 20.25 per cent, and they have remained there since 1923. The radium technique has never been changed in our clinic. We always apply the same amount in the same applicator in the cervical canal. If any improvement occurred it must have been due to the higher voltage roentgen rays. The technique is so simple that it could be used in every clinic where radiation therapy is employed. (Presented slides.) I think the solution of the entire problem is simply a solution of the technique. (Demonstrated applicator.) For instance in fundal cancers a Y-shaped applicator is used. Thereby the radiation tissue dose applied to the uterus is practically homogeneous within the periphery of the organ. Adenocarcinomas will respond to irradiation as well as solid carcinomas. The success of radiation therapy depends entirely on the technique and the tissue radiation dose.

DR. BROOKE M. ANSPACH, Philadelphia. I have been much impressed by the paper of Dr. Healy, by the careful analysis of Drs. Bowing and Fricke, as well as by the report of Dr. Kaplan and the interesting experimental work of Dr. Sittenfield.

Cancer of the cervix may be as successfully treated with radium as with operation and there is practically no mortality. Irradiation has come, therefore, to be the procedure of choice. The prospect for the patient with cancer of the cervix depends upon the stage at which the disease is discovered, the variety of the growth, the resistance of the patient, and, of course, upon the technique of irradiation. My own experience in the treatment dates back to January, 1913, when, following a visit to Dr. Kelly's clinic, I applied radium to a Stage III epithelioma of the cervix. The results were so remarkable that Dr. Clark, whom I had the privilege of assisting at that time, began to use it in advanced cases. I need not detail the variation in the dosage and the methods of application, etc., made from time to time as trial and error suggested, because ours has been the common experience. In the beginning, a capsule of radium placed within the cancerous cervix for twenty-four hours, sometimes a repetition of the dose after six to eight weeks, with the idea of further influence upon an already startling regression of the lesion; later a larger initial dose, the avoidance of curettage or even destructive cauterization; with increasing experience a realization of the risk attending a second large dose and the good derived from removal with the cautery of proliferating masses were some of the noteworthy features. The reports of these earlier cases have been given elsewhere.

I shall speak here of the treatment of cancer of the cervix in the gynecologic ward service at the Jefferson Hospital since 1922. We had 150 cases up to January 15, 1930; of these 140

were treated. At the outset we used irradiation with radium in the early cases and then did a hysterectomy; 2 of this group at the end of five years were cancer-free, but one of them subsequently exhibited a recurrence so that our percentage of salvage was reduced to 25. We soon abandoned hysterectomy and treated all cases with radium alone. The first report of our cancer work was made by my associates Drs. Lewis C. Sheffey and William J. Thudium and is now in press. Every patient has been examined by both men except two—one living now in England and one refusing to come back to the hospital but finally interviewed by the social service worker.

We have not made a histologic classification in this group. All of the operable cases (3) were cancer-free at the end of five years but one at seven years died of cancer.

Of the inoperable group (50), 8 were cancer-free at the end of five years; 6 are cancer-free at present.

Our technique has varied with experience. At first 2,400 milligram-hours, later 3,600 to 4,500; more recently a return to 3,600 mg-hr. The radium salt was used in capsules of platinum, silver or brass, encased in black rubber or in needles of monel metal.

As time went on our feeling against re-irradiation diminished in cases showing an easily accessible recurrence; to them we have made a second application in smaller doses. We have used roentgen irradiation in cases obviously unsuited to a radium technique.

We have been able to follow up 95.7 per cent of the treated cases.

We would like to suggest that all reports of five-year groups be modified from time to time because a definite proportion of these cancer-free cases have recurrences and die later. We would also raise the question of whether a re-irradiated case must not be dated so far as results are concerned from the time of re-irradiation. This would alter some of our five-year radium statistics.

Our absolute five-year curability was 18.6 per cent.

Our relative five-year curability was 20.7 per cent.

The present-day absolute curability is 13.5 per cent.

The present-day relative curability is 15 per cent.

It need hardly be said that the technique and dosage are of much importance. To some extent, at least in our own clinic, it has depended upon our available means. We are inclined to believe that when it is practicable the deep general roentgen therapy of the pelvis should precede the local application of radium. In this way the entire pelvis, including remote areas, will be irradiated and some cancer cells that cannot be reached or that would be missed by the local application of radium will be destroyed.

So far as cancer of the fundus is concerned, we prefer hysterectomy, for obvious reasons. A summary of our experience in this regard has not been made. Our first view, that cancer of the fundus in the early stage is nearly always cured by operation, still holds in good operative risks but taking the patients as they come to the clinic, many with advanced growths and with general complications, the results are not so gratifying.

We agree with Drs. Bowing and Fricke that the method of treatment depends upon the features of the individual case. We have followed the same plan they report. As the diagnosis of the fundus is sometimes questionable even when curettage has been done, from the gross appearance of the tissues, we at once apply radium (50 mg.) in doubtful cases. A histological report is secured within twenty-four hours; if the case is malignant the radium is left in place for twenty-four hours longer (a dose of 2,400 mg-hr.) and six to eight weeks later complete hysterectomy is done. Although no report can now be made we have been pleased with the results of this plan of treatment.

In one case so far advanced as to be considered inoperable and hopeless we used 3,600 mg-hr. of radium. There is no evidence of the disease at the end of seven years.

Dr. P. Brooke Bland, Philadelphia. From the papers presented one is led to conclude that the treatment of uterine carcinoma in this country is almost entirely by radiation therapy. These papers bear out a prophecy I had the temerity to make some years ago, although at the time I was reminded that prognostications are only hopes finding words, and to venture a forecast of what the next decade might bring forth was not only dangerous but was to fly in the face of wisdom. Prior to that period I followed the methods in vogue and practised radical surgery in all cases that fell in the category we nominated operable.

I am heartily in accord with practically all of the statements made by the speakers who have preceded me. They have clearly portrayed the superior value of irradiation in the treatment of uterine malignancy and I believe nearly all workers in this country look upon this recourse as the preferential plan. I have not performed a single radical operation for carcinoma of the cervix for more than ten years, nor, in the light of modern knowledge or from my own experience, could I be persuaded to do so. From the statements made here today, as well as from the information one gathers from the current literature, it seems altogether safe to say that cervical cancer can no longer be regarded as a surgical disease.

While I realize there is a tendency to withdraw carcinoma of the fundus from this category, as indicated by the appearance of numerous articles dealing with the subject, and by the paper presented today by Dr. Bowing and Dr. Fricke, I have been somewhat loath to depart from a custom that almost uniformly eventuates in gratifying ultimate results.

However, I have not employed radium to any extent in the treatment of endometrial malignancy and am not qualified, therefore, to speak of its value in cases of this type. In patients afflicted with carcinoma of the fundus, I still cling rather tenaciously to semiradical surgical means.

Recently, a patient with carcinoma of the endometrium came under my care. I performed, as is my present custom in these cases, a modified Wertheim hysterectomy. The patient had been irradiated on two occasions previously, but her chief symptom (more or less constant bleeding) continued. On sectioning the uterus after operation a "sugar-loaf" mass of malignant disease was found in the right upper quadrant of the organ.

As experience altered my course in treating cervical cancer, it may also change my therapeutic attitude in the care of cancer of the upper segment of the reproductive tract. At the present I should be very reluctant to change and I believe that the best results in carcinoma of the body of the uterus will follow surgical extirpation and of cervical carcinoma irradiation.

In general, in approaching therapeutically cases of uterine cancer my attitude is governed by my own experiences and by the experience expressed by most of my contemporaries. Still more important, however, than the therapy of cervical carcinoma is the prevention and prompt correction of lesions that may ultimately lead to cancer.

Heretofore, it has been customary to stress the value of early diagnosis of the disease. No one will gainsay the merits inherent in this practice. The practical application of this aspect of the problem rests with the gynecologist, but apart from this feature of the subject, there is another which appeals to me as still more important. It falls in the hands of the obstetrician. It is generally conceded that it is almost physically impossible for a woman to give birth to a normally developed full term baby without sustaining some injury of the cervix, and it is common knowledge that more that 80 per cent of parous women suffer with cervical lesions of varying degree inflicted during parturition

The fact that more than 95 per cent of the cases of cancer of the cervix arise in multiparous women cannot be looked upon merely as an incident There must be an intimate etiological relationship and it is generally believed that most cases have their basic origin in parturitional trauma with sequential cell metaplasia incident thereto. This may be regarded as the most definitely known lesion to precede cervical cancer. It may be looked upon as essentially the exciting or secondary cause of the disease. It has, also, been conclusively demonstrated that only in the most exceptional instances does carcinoma develop in damaged cervices when promptly and properly restored following childbirth. Unrepaired cervical lesions must be looked upon as definitely carcinogenic and it is in the obstetric prevention of these that the chief solution of the prophylactic problem lies.

Since, in the final analysis, carcinoma of the cervix is largely an expression of incomplete maternity service, it becomes obvious that the solution of the problem, so far as prevention is concerned, rests almost wholly in the hands of the accoucheur. On him more than any other individual does the matter of prophylaxis fall.

DR. FLOYD E. KEENE, Philadelphia. The treatment of cervical carcinoma must be considered from three standpoints: prophylactic, palliative and curative. It has been said that the time to cure cancer is before it develops, and this applies with particular emphasis to cancer of the cervix. Abundant evidence is at

hand showing that carcinoma is essentially a disease of the traumatized cervix and that cancer rarely develops in a multiparous cervix subsequent to repair or cauterization.

Despite active propaganda against cancer, early lesions of the cervix are rarely seen. In our series, Stage I was present in less than 5 per cent, with Stage III forming by far the largest group, in which palliation rather than cure could be anticipated. In from 60 to 70 per cent of these patients irradiation will be followed by at least temporary cessation of bleeding and foul discharge, with improvement in general health. If radium has accomplished nothing more, the relief it brings to these sufferers has made its advent a boon to humanity. During our early experience with radium, all patients were treated irrespective of the extent of the lesion. This, we believe, is a mistake. Wide parametrial involvement with, perhaps, extension to the bladder or rectum rarely responds favorably to radium, and not infrequently exaggerated suffering follows its use. Furthermore, discredit is cast upon a method which in properly selected cases offers much in the way of relief or cure.

In the John G. Clark Clinic at the University Hospital, irradiation has supplanted operation for cervical cancer during the past fifteen years. We have used radium element in doses varying from 2,400 to 3,000 milligram-hours. In our Stage I cases, we have combined high cautery amputation with irradiation, and in the more advanced lesions, cautery excision of cauliflower masses or cauterization of the crater has preceded the radium application. For several years a second application was given routinely six weeks later, but this was given up since we believe it increased the incidence of fistula formation and did not improve our end-results. These patients are kept under close observation, and radium is re-applied when the local condition indicates its use. It has been, and is still, our opinion that the greatest benefit accrues from the primary treatment.

Our results are as follows: There has been a total salvage after five years of 13.7 per cent. In a small series of Stage I cases, where cautery amputation and radium have been employed, an apparent cure has been obtained in 80 per cent. In Stages I and II, cautery excision and radium have given a 42.9 per cent cure, and where radium alone was used in the same type of lesion, 37 per cent.

Our experience with deep roentgen therapy has been disappointing, but the reports of Dr. Healy and others encourage us to further efforts along this line. Theoretically, the combination of radium and deep roentgen therapy is logical and practically the results indicate its value as a palliative measure. Sufficient data are not available as yet upon which to base deductions regarding its curative value, but we doubt if it will add materially to the total salvage after five years.

Dr. Bowing (closing). I wish to emphasize the importance of grouping cases according to the type of treatment that was carried out, and of keeping in mind the stage of malignant involvement at the time the patients present themselves for treatment. The degree of radiosensitivity varies, as does the accessibility of tissues to effective radium treatment. The results depend on many factors; the age of the patient, the grade of malignancy, the accessibility of the lesion, the extent of local and distant metastasis, and so forth. Surgical intervention should be the first, but not the only consideration. Irradiation, alone or combined with other methods intelligently used in selected cases, should increase the immediate good results, and definitely prolong life following operation.

Dr. Healy (closing). I wish to express to the members who participated in the discussion my appreciation of the trouble they went to, for each of them has given reports of his own work, which had been carefully investigated, and which add greatly to the value of the symposium. I wish to encourage those of you who have not as yet utilized high voltage roentgen therapy in this group of cases, the advanced Group IV cases, to do so. There is no question that you will be gratified by the results.

I agree with Dr. Keene, for I have been unable to see that there is any great difference in the five-year end-results in the cases that are treated by us with all this preliminary roentgen irradiation, or roentgen irradiation after operation, because they depend upon Groups I and II. Two-thirds of the cases are Groups III and IV. The greatest difference is in the first two years. You will get 20 to 22 per cent of total absolute salvage, according to the literature, and in our own personal experience, whether you are treating these cases by roentgen irradiation plus radium, or by roentgen irradiation plus radium plus hysterectomy, or by

radical surgery alone, you will get approximately, in the hands of the most expert surgeon and the competent radiologist about 20 to 22 per cent five-year results. The advantage of radiation therapy is the lack of mortality in the treatment of the 2 out of 3 cases that are too advanced for surgery, and the increased longevity in all the cases. After you get into the fourth, fifth and sixth years, the percentages run along just the same, no matter what method is employed. This is the important thing to bear in mind. I have studied the statistics of men where they use no radiation, where they use radiation in the canal only, and the statistics of Dr. Schmitz, who uses no vaginal irradiation, and the statistics of Heyman. We all finally wind up with about 20 per cent total salvage at the end of five years.

A PIONEER ROENTGENOLOGIST*

EUGENE ROLLIN CORSON, M.D., SAVANNAH, GEORGIA

By E. H. SKINNER, M.D.
KANSAS CITY, MISSOURI

"The poor and the humble have been my chief patients, but I do not regret it, for I have gotten great pleasure out of my work."

"There is not one of the sciences which has made the strides which have taken place in x-ray and molecular physics, the real fairy tales of science; and think of the next hundred years when even more willing ears will listen to the greater fairy tales of science, when you and I, like streaks of morning clouds, shall have faded away into the infinite azure of the past."

DR. EUGENE ROLLIN CORSON was born in Washington, D.C., July 20, 1856. He was educated at private schools and St. John's College, Annapolis, Md. He entered Cornell University in 1871 in the science course and graduated with the degree of B. S. in 1875. He received his first medical degree in the Hahnemann Medical College in Philadelphia in 1877. He took a second medical degree at the Southern Medical College at Atlanta, Ga., in 1894.

He was house physician in the Ward's Island Hospital, New York, in 1878. He took his post-graduate course in Vienna, Austria, in 1878–1879. His studies were much interfered with by serious illness. He went South on account of very delicate health and located at Savannah, Ga., in October, 1879, where he has practised ever since.

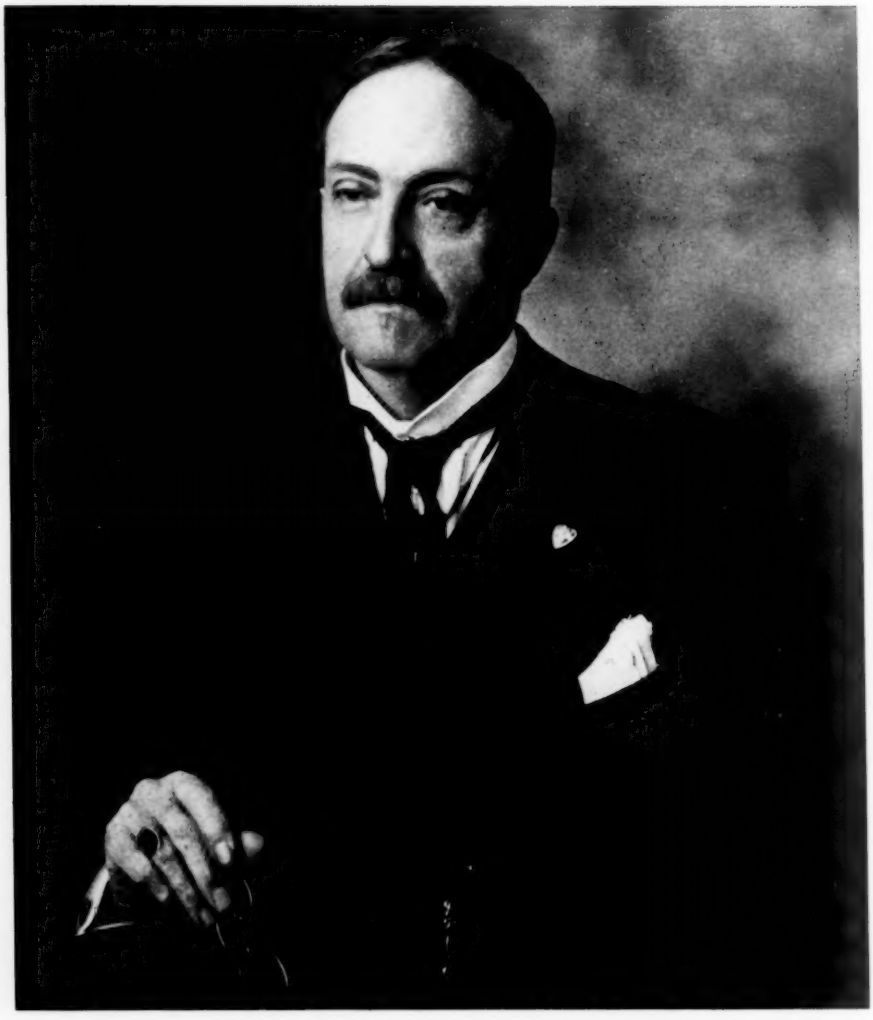
"In November, 1895, I (Corson) picked up at a news-stand a copy of the New York Staat-Zeitung with a description of the discovery of the x-ray by Professor Roentgen. I had had floating through my mind a method of seeing some of the bones by a fluorescent paint on the body viewed in a dark room by a concentrated beam of light, and now I saw that vision ten thousand times amplified by this discovery. I had in my office a little high tension coil energized by a 50 cell Edison battery. I got from Queen & Co. of Philadelphia an original Crookes tube. I had long been familiar with Sir William Crookes' experiments with electrical discharges through a more or less high vacuum and his theory of radiant matter. Although he failed to discover the x-ray, his work opened up an immense field for experimentation and future discoveries. I have always regretted that the discovery had to pass to others, for really the discovery was accidental, though this in no way lessens the brilliant work of Professor Roentgen. My little coil which I still possess, was for therapeutic purposes, and gave a spark, at best, of $\frac{1}{4}$ inch. I put a key and a coin on a plate and played on it for a half hour, and on development got a very fair picture.

"It did not take me long to get a 10 inch Ruhmkorff coil and soon thereafter a 15-inch coil and my x-ray work was started in the spring of 1896."

Dr. Corson early saw the necessity of more amperage and stronger tubes to stand the heavier currents, and he pointed this out in his earlier papers and hailed with joy the first Snook transformer as the realization of this dream.

"In 1902, Dr. Williams of Boston published his work on 'Roentgen Rays in Medicine and Surgery'. This I (Corson) reviewed rather sharply on the ground that he placed the influence machine (Holtz) on the same footing with the induction coil. I tried to show that such advice was very deceptive for the Holtz machine gave a certain high voltage and very little amperage, and that future advance of the science of x-ray would be the production of fatter and heavier sparks and heavier tubes to stand the current. The twenty-eight years which have gone by have amply verified my prediction."

* Prepared from various sources and from personal correspondence.



Eugene Rollin Corson, M.D.

Albers-Schönberg in 1910 published his great work "Die Röntgentechnik." He was the first to construct a coil which could be tapped for different voltages and amperages.

"When Snook came out with his transformer I (Corson) cried out, 'There's my man!' I have one of the original Snook machines and I can take a chest at 6, 8, and 10 feet in 1/10 second and get practically the exact size and shape of the heart and lung detail unsurpassed by any other technique."

While Dr. Corson was preparing his paper on the normal movements of the carpal bones, a work not previously done, the exposure before the fluoroscope, after a long delay of ten years, showed up with epitheliomata on the four fingers of his left hand, three of which were subsequently amputated. At the earnest advice of Professor Halsted, of the Johns Hopkins Hospital, he had all the lymph glands removed from the axilla, and he feels assured that this timely operation has prevented the spread of the malignancy. He would earnestly advise all sufferers from over-exposure to adopt this radical measure.

The loss of his fingers debarred him from further surgical practice. He firmly believes that had his coworkers at that time (and he has in mind especially his friend Dr. E. W. Caldwell, whose early death was an irreparable loss to our profession) who have since given their lives to science, had had the advantage of this early radical treatment they might still be among us today.

He used to meet Caldwell in a little surgical instrument shop just off Fifth Avenue where he had on display his x-ray prints. He also met him at the meetings of the American Electro-Therapeutic Association and Caldwell's charming personality is one of his cherished memories.

In spite of his malignant trouble Dr. Corson's general health has not been affected, and now at the age of nearly seventy-six (1931) he is still active and vigorous and equal to any amount of work.

Indicative of the ingeniousness and originality of Dr. Corson is the following anecdote:

"To show how one can just miss making a discovery (in my case certainly from lack of wits) I shall relate the following incident. A hydrocephalic baby, about eight or ten months old, was brought to my office for treatment. With a trocar I let out the fluid and injected the ventricles with oxygen gas until the head was as tight as a drum. My idea was that possibly the closure of the foramen of Magendie had something to do with the hydrocephalus and that pressure of the air in the ventricles might open up the foramen. Although I had my x-ray outfit at hand it did not occur to me that the x-ray would outline the ventricles, and I missed being the discoverer of ventriculography. I mentioned this to my friend Dr. Walter E. Dandy, the distinguished brain surgeon, and he was much interested and mentioned it in one of his lectures. Alas! So many of us poor mortals lack the wits!"

Dr. Corson's first paper dealing with the roentgen ray appeared in the *New York Medical Record*, May 8, 1897. This was on Colles' fracture, and in October, 1897, he published one on x-ray technique.

Dr. Corson published a paper in October, 1898, in the *Annals of Surgery* on a "Rare Form of Bone Atrophy following an Ununited Fracture." In December, 1898, in the *Proceedings of the Association of American Anatomists* he published a paper on the "Normal Movements of the carpal Bones and Wrist." This paper was well received and was the first attempt to show definitely the functioning of the carpal bones and that they really moved as two rows and not as a cluster.

In December, 1899, he published in the *Annals of Surgery* a paper entitled "A Skiagraphic Study of the Normal Membral Epiphyses at the Thirteenth Year." This paper was read in New York before the American Electro-Therapeutic Association and Dr. Caldwell honored Dr. Corson by pronouncing the skiagraphs the best he

had ever seen. "As I look back over this work and remember the long exposures necessary—five minutes for the hand and elbow—I am surprised at my results. It was about this time that the Germans were shortening the time of exposure with intensifying screens and Donan, of Germany, was obtaining roentgenograms of hips in only 20 seconds. I mentioned this to Dr. Caldwell and he was very much surprised."

This paper was reviewed at length in England by John Poland whose work on the epiphyses, a very large volume, was a mile-stone on the road to the present wonderful advance in the science of roentgenology.

Dr. Corson wrote again, in 1900, a paper which was published in the *Proceedings of the Association of American Anatomists* on the "Value of the X-ray in the Study and Demonstration of Normal Anatomy." In 1901 he published a paper on the technique to bring out bone detail.

In April, 1902, he published a paper on bone cysts, and reported a cyst he had operated on and cured. This was the first x-ray paper on the subject published in this country.

In 1902 he demonstrated at Cornell University, with lantern slides, the value of the roentgen ray in the study of normal anatomy and especially of the membral epiphyses and the growth of bone. He has been a member of the Association of American Anatomists, the American Electro-Therapeutic Association, of his local and State societies, the American Medical Association and the American Roentgen Ray Society. He has been a close student of roentgen-ray work in Germany and regards the German workers as unexcelled in their discoveries and research, and as having produced the greatest literature on the subject.

"From the very beginning . . . the Germans have published the best works on the x-ray and it is mostly from them that I owe what knowledge I possess of the theory and practice of the x-ray. If France has been a little slow in its x-ray publications it has certainly caught up with the profession in this beautiful volume, to wit, "Anatomie Radiographique in Squelette Normal (Atlas) par J. Belot et F. Lepennetier, Paris."

"Die Roentgenographie in Der Innere Medicine," by Von Ziemssen and H. Rieder, Wiesbaden, 1902, 3 volumes. "This is the first work which demonstrated the value of the intensifying screen. The skiagraphs showing the very characteristic picture of tertiary syphilis in bone are fine and as typical of diagnosis as the Wassermann test."

"Roentgenologische Studien über der Bulbus Duodeni mit Besonderer Berücksichting der Diagnostik des Ulcus Duodeni" von Ake Akerlund, Stockholm, 1920 (Supplement I, *Acta radiologica*) "The best work ever written on the subject."

In April, 1905, Dr. Corson published a paper on a case of ureteral stone which he had located and operated upon. This was at least the first case in Savannah, so operated on and cured.

PARTIAL BIBLIOGRAPHY OF EUGENE ROLLIN CORSON

1. Some observations on Colles' fracture by the aid of the x-ray. *Med. Rec.*, 1897, *51*, 649–653.

2. Some hints on x-ray work. (With special reference to rheumatic conditions and the comparative shadows of calcium carbonate, calcium phosphate, urate of soda, and bone dust.) *Georgia J. M. & S.*, 1897, *1*, 133–138.

3. A case of Colles' fracture treated prone on a flat splint with chief regard to ruptured ligaments. *Med. Rec.*, 1898, *53*, 82–83.

4. A rare form of bone atrophy following an ununited fracture as seen by the x-ray. (A case of excessive bone atrophy complication, an ununited fracture in both forearms of the same individual.) *Ann. Surg.*, 1898, *28*, 503–508.

5. An x-ray study of the normal movements of the carpal bones and wrists. *Proc. Ass. Am. Anat.*, 1898, *11*, 67–92.

6. The mechanism of fracture of the neck of the radius. *Ann. Surg.*, 1899, *30*, 691–695.

7. A skiagraphic study of the normal membral epiphyses at the thirteenth year. *Ann. Surg.*, 1900, *32*, 621–647.

8. The value of the x-ray in the study and demonstration of normal anatomy. *Proc. Ass. Am. Anat.*, 1900, *14*, 43–46.

9. The x-ray and photographic technique necessary to bring out bone details in the print. *Ann. Surg.*, 1901, *34*, 560–566.

10. Bone cysts. (A case in which the humerus was involved, with the x-ray and microscopic findings. This was the first paper on this subject in this country. There was only a scant bibliography on the subject from European workers, almost wholly German.) *Ann. Surg.*, 1902, *35*, 505–511.

11. A case of ureteral calculus located by x-ray and removed successfully by transperitoneal abdominal section operations. (First case operated on in Savannah.) *Georgia Pract.*, 1905, *1*, 109–112.

12. X-ray findings in a case of Gritti-Stokes' Amputation. *Ann. Surg.*, 1906, *43*, 750–752.

13. Skiagraphs illustrating certain bone lesions and the x-ray technique necessary to bring out the bone details. *Georgia Pract.*, 1905, *1*, 11–13.

14. An x-ray study of bone atrophy. *Ann. Surg.*, 1910, *51*, 289–299.

15. A medico-legal case involving x-ray testimony and its bearing on a recent proposal to regulate medical expert testimony. *South M. J.*, 1908, *1*, 82–89.

16. Fusion of the semi-lunar and cuneiform bones in both wrists of an adult negro, shown by the x-ray. *Anat. Rec.*, 1908–1909, *2*, 143–146.

17. X-ray apparatus and x-ray methods and the lines along which progress has been made. *Med. Age*, 1902, *20*, 801–809.

18. Some thoughts on Crookes' tubes. *Tr. Am. Electro-Therapeutic Ass.*, 1899–1900.

19. X-ray photography. *Tr. Am. Electro-Therapeutic Ass.*, 1899–1900, 378–387.

20. Some thoughts and suggestions on x-ray work. *Tr. Am. Electro-Therapeutic Ass.*, 1897.

COLLATERAL INTERESTS AND PUBLICATIONS

While Dr. Corson seems to constantly maintain his passion for roentgenologic practice, he has been much interested in many problems of surgery and obstetrics. He has collected, enjoyed and discussed by essays many other subjects as is witnessed by this incomplete catalogue of publications:

1. The vital equation of the colored race and its future in the United States. A lecture delivered before the Georgia Historical Society, June 1887. This lecture, much elaborated, appeared in the *Wilder Quarter-Century Book*, Cornell University, 1893.

2. Some clinical jottings on our Southern fevers and their treatment. *New York Med. Times*, 1890, *18*, 1–5.

3. Some clinical jottings on twenty cases of puerperal eclampsia. *Med Rec.*, 1891, *40*, 502–506.

4. A suggestion in the operation of vesico-vaginal fistula. *Am. J. Obst.*, 1894, *30*, 209–212. (Also reprinted in England.)

5. The Apostoli treatment of uterine fibroids, a report of nine cases. *Am. J. Obst.*, 1895, *32*, 341–348. (Translated into French by Apostoli.) "In this paper I measured the galvanic current through a copper electrode in the uterus and the clay pad on the abdomen by means of a Wheatstone bridge giving the resistance in ohms as well as the amperage through an ammeter. Currents were used up to half an ampere under anesthesia. Apostoli claimed that the cure was only symptomatic, but in one case I was able to demonstrate that in the subsequent operation for appendicitis the fibroid had absolutely disappeared, showing a complete uterine debacle. This case is unique in medical literature."

6. Some clinical jottings on five hundred cases of labor. *Am. J. Obst.*, 1897, *35*, 175–196; 364–392.

7. A simple exploratory laparotomy as a palliative and perhaps curative measure in inoperable carcinoma of the breast, preliminary report of a case, March, 22, 1902.

8. Sequel to above paper, the oxygen bath for the peritoneum and its possible value, second report on the cancer case relieved by an exploratory laparotomy. *Am. Med.*, 1902, *4*, 734.

9. Narath's modification of Talma's operation for hepatic cirrhosis; report of a successful case. *Ann. Surg.*, 1907, *46*, 831–840.

10. The Centennial Anniversary of the Georgia Medical Society, an Historical Review (privately printed), 1905.

11. A torn cervix versus uterine inertia. *Med. Rec.*, 1918, *94*, 239–241.

Among Dr. Corson's cherished possessions is a fine collection of Sir Charles and John Bell and his collection of anatomies and upon the history of medicine. From this material he has contributed several papers which have been read before historical societies:

12. Sir Charles Bell, the man and his work. Paper read before the Johns Hopkins Hospital Historical Society, June 1910. *Johns Hopkins Hosp. Bull.*, 1910, *21*, 171–182.

13. John Bell, Surgeon. Paper read before the Johns Hopkins Hospital Historical Society. *Johns Hopkins Hosp. Bull.*, 1912, *23*, 241–250.

14. Some unpublished water color sketches of Sir Charles Bell with observations on his artistic qualities. Paper read before the International Medical Congress in London, August 7, 1913. *Johns Hopkins Hosp. Bull.*, 1914, *25*, 185–189.

"It warmed the cockles of my heart to meet men who were interested in the science of medicine and not its mere everyday practice."

15. Agassiz's essay on classification fifty years after. *Scient. Month.*, 1920, *11*, 43–52.

16. Some unpublished letters of Helena Petrovna Blavatsky, with Introduction and Commentary, Rider and Co., London, England, 1928.

17. Pneumonic toxaemia vs. the theory of obstruction in pneumonia. *Georgia J. M. & S.*, 1897, 1, 220–229.

18. Clinical types of melena as seen in Savannah. *Georgia J. M. & S.*, 1898, *2*, 163–174.

19. Encouraging the surface growth of carcinoma as a palliative measure of treatment. *Georgia J. M. & S.*, 1898, *2*, 109–111.

20. The danger of chloroform anesthesia by gaslight. *Atlanta M. & S. J.*, 1898–1899, *15*, 326.

21. Value of ergot in diseases of the prostate. *Atlanta Jour.-Rec. Med.*, 1900, *11*, 246–249.

22. A large pelvic extraperitoneal hematocele following dilatation of the cervix and curettage. *Am. J. Obst.*, 1901, *42*, 516–519.

23. The x-ray technic of Dr. H. Albers Schönberg. *New York M. J.* 1904, *79*, 65–69.

24. A retrospect of men and events in the medicine of the past 100 years. *Georgia Pract.*, 1905, *1*, 75–78.

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THE AMERICAN JOURNAL OF ROENTGENOLOGY AND RADIUM THERAPY

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EDITORIALS

DIAGNOSIS OF PRECANCEROUS LESIONS OF THE COLON

STEWART, in his Croonian Lectures[1] delivered before the Royal College of Physicians of London in June, 1931, called attention to the precancerous lesions of the alimentary tract, emphasizing the fact that the outstanding example of a definitely precancerous lesion of a benign neoplastic kind is the adenomatous polyp of the colon, rectum and stomach. It is only within recent years, however, that the very considerable frequency of intestinal polypi and their pronounced tendency to malignant change have come to be adequately recognized. The importance of recognizing these polypoid lesions of the colon roentgenographically in the light of their tendency to become malignant cannot be too strongly emphasized. Polypoid lesions of the colon, however, as Weber[2] has pointed out, cannot be depended upon to produce roentgenographically demonstrable deformities in the lumen of the colon, especially in the routine roentgen examination of the colon as ordinarily practised. Weber has, by varying the roentgen technique, been able to demonstrate polypoid lesions and polyposis of the large intestine. His technique consists in the use of a combined method, as suggested by Fischer,[3] comprising the use of a contrast medium in association with insufflation of air. Since the early days of roentgenology gases have been introduced into the colon to serve as a contrast medium and clinicians have for a long time inflated the colon in order to demonstrate its relation to adjacent abdominal tumor masses. But it has only been relatively recently, since the work of Fischer, Gershon-Cohen,[4] Weber, and others, that the use of air in association with metallic salts has yielded results practical enough to warrant its more widespread application. The employment of this technique permits the visualization of the contours of the intestine without obscuring or destroying intraluminal relief, and polypoid tumors which occur singly or relatively sparsely are visualized as rounded soft projections into the intestinal lumen, their contours being outlined strikingly in the air-distended bowel, and when sufficient care has been exercised in carrying out the technique, it enables a determination of the nature of the surface contours of the growth and affords an estimate of the integrity of the interior of the colon obtainable by no other method except direct visualization by the proctosigmoidoscope or surgical or post-mortem exploration. Since the method offers an opportunity of demonstrating these precancerous lesions its employment deserves a more widespread use, and while, as Weber says, the method may not be practical as a routine procedure, it offers a distinct advance over the ordinary method of examination in cases in which a lesion is suspected and the routine enema examination is not sufficiently conclusive. The greater frequency of diagnosis of these pracancerous lesions would, it is believed, lessen the incidence of malignant disease of the colon and any method which contributes to a more accurate diagnosis of these somewhat obscure conditions deserves and should receive more general application among roentgenologists.

[1] Stewart, Matthew J. Precancerous lesions of the alimentary tract. *Lancet*, 1931, *2*, 565–572; 617–622; 679–674.

[2] Weber, Harry M. The roentgenological demonstration of polypoid lesions and polyposis of the large intestine. AM. J. ROENTGENOL. & RAD. THERAPY, May, 1931, *25*, 577–589.

[3] Fischer, A. W. Ueber die Röntgenuntersuchung des Dickdarms mit Hilfe einer Kombination von Lufteinblasung und Kontrasteinlauf ("kombinierte Methode"). *Arch. f. klin. Chir.*, 1925, *134*, 209–269.

[4] Gershon-Cohen, J. The diagnosis of early ileocecal tuberculosis; preliminary report with special reference to the double contrast enema. AM. J. ROENTGENOL. & RAD. THERAPY, 1930, *24*, 367–388.

WALTER B. CANNON ANNIVERSARY

ON OCTOBER 15, 1931, in Boston, was celebrated the completion by Walter B. Cannon of twenty-five years of service as George Higginson Professor of Physiology in the Medical School of Harvard University. In the afternoon addresses were made by Dean Edsall of the Harvard Medical School, Dr. Walter C. Alvarez of of the Mayo Clinic and Dr. William H. Howell, Professor of Physiology, emeritus, the Medical School of the Johns Hopkins University.

In the evening in the gymnasium of Vanderbilt Hall (the dormitory of the Medical School) Dr. Cannon's friends tendered him a dinner and presented to the University Dr. Cannon's portrait. President Lowell presided as toastmaster and Dr. Graham Lusk, Professor of Physiology, School of Medicine, Cornell University, made the address of the evening. Dr. Cannon responded in his own delightful, inimitable manner.

Dr. Cannon is not only an outstanding figure in American physiology both as a teacher and investigator but in addition in a very striking way has participated in the intellectual activities of numerous large groups of men primarily concerned in the problems of clinical medicine and has contributed fundamental knowledge and significant methods to help them in the solution of these problems.

For roentgenologists his early utilization of the roentgen ray in the study of the gastrointestinal tract opened the way to the present daily use in every corner of the world of the roentgen ray in the diagnosis of diseases of the gastrointestinal tract. While still a student in the medical school his first observations were made, and they were published as early as 1898 in papers entitled "The Movements of the Stomach Studied by Means of the Roentgen Rays," *Am. J. Physiol.*, 1898, *1*, 359, and "The Movements of the Food in the Esophagus," *Am. J. Physiol.*, 1898, *1*, 435.

Thus early in his career contacts with those using physiological investigation in application to the solution of clinical problems were made and ever since he has maintained a close association with clinicians and roentgenologists, an association profitable to them and rendered exceedingly pleasant by reason of a genial personality radiating good humor. All of these join with the physiologists and the students and teachers of his medical school in felicitating Dr. Cannon on his fruitful service during his twenty-five years of professorship at the Harvard Medical School.

HENRY A. CHRISTIAN

As this number goes to press, we regret to announce the death of Professor Guido Holzknecht, head of the Vienna Roentgen Institute, which occurred on October 30. An account of Dr. Holzknecht's life and work will appear in an early issue of the Journal.

SOCIETY PROCEEDINGS, CORRESPONDENCE AND NEWS ITEMS

Items for this section solicited promptly after the events to which they refer.

MEETINGS OF ROENTGEN SOCIETIES*

UNITED STATES OF AMERICA

AMERICAN ROENTGEN RAY SOCIETY
Secretary, Dr. E. P. Pendergrass, University Hospital, Philadelphia, Pa.
Thirty-third annual meeting: Detroit, Mich., 1932.

AMERICAN COLLEGE OF RADIOLOGY
Secretary, Dr. Albert Soiland, 1407 S. Hope St., Los Angeles, Calif.
Annual Meeting: New Orleans, La., 1932.

SECTION ON RADIOLOGY, AMERICAN MEDICAL ASSOCIATION
Secretary, Dr. G. W. Grier, Jenkins Arcade, Pittsburgh, Pa.
Annual meeting: New Orleans, La., May 9-13, 1932.

RADIOLOGICAL SOCIETY OF NORTH AMERICA
Secretary, Dr. I. S. Trostler, 812 Marshall Field Annex, Chicago, Ill.
Seventeenth annual session: Hotel Jefferson, St. Louis, Mo., Nov. 30–Dec. 4, 1931.

RADIOLOGICAL SECTION, LOS ANGELES COUNTY MEDICAL SOCIETY
Secretary, Dr. John F. Chapman, 209 Professional Bldg., Pasadena, Calif.
Meets on the third Wednesday of each month at the California Hospital.

RADIOLOGICAL SECTION, SOUTHERN MEDICAL ASSOCIATION
Secretary, Dr. W. S. Lawrence, Medical Arts Bldg., Memphis, Tenn.

BROOKLYN ROENTGEN RAY SOCIETY
Secretary, Dr. J. J. Masterson, 401-76th St., Brooklyn, N.Y.
Meets monthly on the first Tuesday from October to April.

BUFFALO RADIOLOGICAL SOCIETY
Secretary-Treasurer, Dr. Joseph S. Gian-Franceschi, 610 Niagara St.
Meets second Monday of each month except during the summer months, the place of meeting to be selected by the host.

CHICAGO ROENTGEN SOCIETY
Secretary, Dr. George M. Landau, 660 Groveland Park.
Meeting second Thursday of each month October to May inclusive at Virginia Hotel.

CLEVELAND RADIOLOGICAL SOCIETY
Secretary, Dr. A. Srauss, 518 Medical Arts Bldg.
Meetings are held at 6:15 P.M. at the Cleveland Chamber of Commerce Club rooms on the fourth Monday of each month from October to April, inclusive.

DETROIT ROENTGEN RAY AND RADIUM SOCIETY
Secretary, Dr. E. R. Witwer, Harper Hospital.
Meets monthly on first Thursday from October to May, at Wayne County Medical Society Building.

ILLINOIS RADIOLOGICAL SOCIETY
Secretary, Dr. Fauntleroy Flinn, 220 South Webster St., Decatur, Ill.
Regular meetings held quarterly.

INDIANA ROENTGEN SOCIETY
Secretary, Dr. J. N. Collins, Indianapolis, Ind.
Annual meeting each February 22 in Indianapolis.

MILWAUKEE ROENTGEN RAY SOCIETY
Secretary, Dr. J. E. Habbe, 221 Wisconsin Ave., Milwaukee.
Meets first Friday in October, December, February and April.
Place of meeting designated by the president.

MINNESOTA RADIOLOGICAL SOCIETY
Secretary, Dr. L. G. Rigler, University Hospital, Minneapolis, Minn.
Next meeting: Minneapolis, Minn., February, 1932.

NEW ENGLAND ROENTGEN RAY SOCIETY
Secretary, Dr. Thomas R. Healy, 370 Marlboro St., Boston, Mass.
Meets monthly on third Friday, Boston Medical Library.

NEW YORK ROENTGEN SOCIETY
Secretary, Dr. J. Bennett Edwards, Englewood Hospital, Englewood, N. J.
Meets monthly on third Monday, New York Academy of Medicine, at 8:30 P.M.

CENTRAL NEW YORK ROENTGEN RAY SOCIETY
Secretary, Dr. Robert C. Hall, 258 Genesee St., Utica, N.Y.
Three meetings a year—January, May and November.

PENNSYLVANIA RADIOLOGICAL SOCIETY
Secretary, Dr. W. E. Reiley, Clearfield, Penna.
Next meeting, to be announced.

PHILADELPHIA ROENTGEN RAY SOCIETY
Secretary, Dr. Karl Kornblum, 3400 Spruce St.
Meeting first Thursday of each month from October to May inclusive, at 8:15 p.m., in Thomson Hall, College of Physicians, 19 S. 22d St.

ROCHESTER ROENTGEN RAY SOCIETY, ROCHESTER, N. Y.
Secretary, Dr. Camp C. Thomas, 476 Lake Ave.
Meets monthly on the first Friday evening at 7:45 at the Rochester Medical Association Building.

ST. LOUIS ROENTGEN CLUB
Secretary-Treasurer, Dr. E. W. Spinzig, 316 Metropolitan Bldg.
Meets first week of each month. Time and place of meetings designated by president.

TEXAS RADIOLOGICAL SOCIETY
Secretary-Treasurer, Dr. C. P. Harris, Houston, Texas.
Meets annually one day preceding the meeting of the Texas State Medical Association.

UNIVERSITY OF MICHIGAN ROENTGEN RAY SOCIETY
Secretary, Dr. C. C. Taylor, University Hospital, Ann Arbor, Mich.
Meets first and third Monday evening of the month from October to June, at 8 o'clock in the amphitheatre of the University Hospital.

* Secretaries of societies not here listed are requested to send the necessary information to the Editor.

Virginia Roentgen Ray Club
Secretary, Dr. Wright Clarkson, 205 S. Sycamore St., Petersburg, Va.
Next meeting, to be announced.

Cuba

Sociedad Cubana de Radiologia y Fisioterapia
Secretary, Dr. Francisco Padron, Enrique Villuendas 64, Havana, Cuba. Meets monthly in Havana.

British Empire

British Institute of Radiology Incorporated with the Röntgen Society
Meets on the third Thursday of each month, from November to June inclusive, at 8:15 P.M., at 32 Welbeck St., London, W. 1., or as advertised.

Electro-Therapeutic Section of the Royal Society of Medicine (Confined to Medical Members)
Meets on the third Friday of each month during the winter at 8:30 P.M. at the Royal Society of Medicine, 1 Wimpole St., London, W. 1.

Section of Radiology and Medical Electricity, Australasian Medical Congress
Secretary, Dr. H. M. Cutler, 139 Macquarie St., Sydney, New South Wales.

Radiological Section of the Victorian Branch of the British Medical Association
Secretary, Dr. Colin Macdonald, Lister House, 61 Collins St., Melbourne, Australia.
Meets monthly at Melbourne during the winter.

Section on Radiology, Canadian Medical Association
Secretary, Dr. A. H. Rolph, 160 St. George St., Toronto, Ont.

Radiological Section, New Zealand British Medical Association
Secretary, Dr. P. C. Fenwick, The Hospital, Christchurch. Meets annually.

Continental Europe

Belgian Society of Roentgenology
Secretary, Dr. J. Boine, Avenue des Alliés, 134, Louvain (Belgium).
Meets monthly on second Sunday at d'Egmonds Palace, Brussels, except in the summertime.

Societe de Radiologie Médicale de France
Meets monthly on second Tuesday, except during months of August and September, 12 Rue de Seine, Paris.

Société Suisse de Radiologie (Schweizerische Röntgen-Gesellschaft)
Secretary for French language, Dr. A. Grosjean, La Chaux de Fonds.
Secretary for German language, Dr. Scheurer, Molzgasse, Biel.
Meets annually in different cities.

Société Francaise d'Electrothérapie et de Radiologie Médicale.
Meets monthly on fourth Tuesday, except during months of August and September, 12 Rue de Seine, Paris.

Association of German Roentgenologists and Radiologists in Czecho-Slovakia
Secretary, Dr. Walter Altschul, German University, Prague, 11/52.

Deutsche Röntgen-Gesellschaft (Gesellschaft für Röntgenkunde und Strahlenforschung)
Meets annually in April, alternating one year in Berlin, one year in some other German city. Meets in addition every two years with the Gesellschaft deutscher Naturforscher und Aerzte.
Permanent secretary, Professor Dr. Haenisch, Klopstockstrasse 10, Hamburg, Germany.

Süd- und Westdeutsche Röntgengesellschaft
Meets annually in different cities.

Nord- und Ostdeutsche Roentgengesellschaft
Meets annualy in different cities.

Dutch Society of Electrology and Roentgenology
Holds two meetings a year in Amsterdam, one in the Spring, and one in the Fall.

Societa Italiana Radiologia Medica
Secretary, Professor M. Ponzio, University of Turin, Turin.

Societatea Romana de Radiologie si Electrologie
Secretary, Dr. Nicolae Busila, 44 Elizabeta Blvd., Bucarest.
Meets second Monday in every month with the exception of July and August.

All-Russian Roentgen Ray Association, Leningrad, USSR in the State Institute of Roentgenology and Radiology, 6 Roentgen St.
Secretaries, Drs. S. A. Reinberg and S. G. Simonson.
Meets annually.

Leningrad Roentgen Ray Society
Secretaries, Drs. S. G. Simonson and G. A. Gusterin.
Meets monthly, first Monday at 8 o'clock, State Institute of Roentgenology and Radiology, Leningrad.

Moscow Roentgen Ray Society
Secretaries, Drs. L. L. Holst, A. W. Ssamygin and S. T. Konobejevsky.
Meets monthly on the first Monday at 8 o'clock, the place of meeting being selected by the Society.

Polish Society of Radiology
Secretary, Dr. Jan. Kochanowski, 45 Gornoslazka St., Warsaw. Meets annually.

Warsaw Section, Polish Society of Radiology
Secretary, Dr. B. Krynski, 11 Zielna St.
Meets once a month except in the summertime.

Scandinavian Roentgen Societies
The Scandinavian roentgen societies have formed a joint association called the Northern Association for Medical Radiology, meeting every second year in the different countries belonging to the Association. Each of the following societies, with exception of the Denmark Society, meets every second month except in the summertime:

Society of Medical Radiology of Sweden
Meets in Stockholm.

Society of Medical Radiology in Norway
Meets in Oslo.

Society of Medical Radiology in Denmark
Secretary, Dr. G. Biering, Copenhagen.
Meets on the second Wednesday of each month from October to July in Copenhagen, at 8 o'clock in the State Institute of Roentgenology.

Society of Medical Radiology in Finland
Meets in Helsingfors.

Vienna Society of Roentgenology
Secretary, Professor Holzknecht, Vienna, IX, General Hospital.
Meets first Tuesday each month, October to July.

Orient

Japan X-Ray Association
c/o Orthopedic Surgery, Tokyo Imperial University.
Meets annually in April.

Kinki Roentgen-Abend Society
Director, Dr. Prof. Taiga Saito, Ogawaoike Tyoto, Japan. Meets bi-monthly on third Sunday.

MINNESOTA RADIOLOGICAL SOCIETY

A joint meeting of the Minnesota Radiological Society, the Iowa X-ray Club and the Radiological Section of the Wisconsin State Medical Society was held at the Mayo Clinic, Rochester, Minnesota, October 17, 1931. The Societies were honored by the presence of Dr. Charles H. Mayo, who delivered an address of welcome, and Dr. Lewis Gregory Cole of New York, who was the guest speaker. The following program was presented.

1. Round table discussion of Gastrointestinal diseases. Conducted by Dr. Lewis Gregory Cole, New York.
2. Benign tumors of the stomach. Dr. Leo G. Rigler, Minneapolis. Discussed by Drs. L. G. Cole, J. D. Camp, C. G. Sutherland.
3. Fractures about the ankle joint. Dr. M. S. Henderson, Rochester. Discussed by Drs. W. H. Ude and G. T. Nordin.
4. Results of radiation therapy in carcinoma of the skin. Dr. L. G. Erickson and Dr. K. W. Stenstrom, Minneapolis. Discussed by Drs. Gage Clement, Hamilton Montgomery and S. W. Harrington.
5. Intrathoracic tumors. Dr. S. W. Harrington, Rochester. Discussed by Drs. C. H. Mayo and L. G. Rigler.
6. Tuberculosis in children. Dr. T. A. Burcham, Des Moines. Discussed by Drs. E. S. Hewitt, Arnold Anderson, L. G. Rigler.
7. Bone changes in hyperparathyroidism. Dr. John D. Camp, Rochester. Discussed by Drs. J. de J. Pemberton and R. M. Wilder.

Following the banquet the principal address of the meeting was delivered:

Correlation of the Roentgenologic Appearance with the Pathologic Changes of Gastric Ulcer.

Dr. Lewis Gregory Cole, New York.

LEO G. RIGLER, *Secretary*,
Minnesota Radiological Society

THE AMERICAN COLLEGE OF PHYSICIANS

The American College of Physicians will hold its Sixteenth Annual Clinical Session at San Francisco with headquarters at the Palace Hotel, April 4–8, 1932. Following the Clinical Session, a large percentage of the attendants will proceed to Los Angeles where a program principally of entertainment will be furnished April 9, 10 and 11.

Announcement of the dates is made particularly with a view not only of apprising physicians generally of the meeting, but also to prevent conflicting dates with other societies that are now arranging their 1932 meetings.

Dr. S. Marx White, of Minneapolis, is President of the American College of Physicians, and will arrange the Program of General Sessions. Dr. William J. Kerr, Professor of Medicine at the University of California Medical School, San Francisco, is General Chairman of local arrangements, and will be in charge of the Program of Clinics. Dr. Francis M. Pottenger, of Monrovia, is President-Elect of the College, and will be in charge of the arrangements at Los Angeles. Mr. E. R. Loveland, Executive Secretary, 133–135 S. 36th Street, Philadelphia, Pa., is in charge of general and business arrangements, and may be addressed concerning any feature of the forthcoming Session.

MEMORIAL TO DR. HICKEY

The many friends of the late Preston M. Hickey will be interested in the announcement that a silver plaque will be presented in his memory by the American Roentgen Ray Society to the University of Michigan at four o'clock on the afternoon of the tenth of December at the Lydia Mendelssohn Theater, Ann Arbor, Michigan. The presentation of the plaque will be made by Dr. A. W. Crane and will be accepted on behalf of the University by President Alexander Ruthven.

BOOK REVIEWS

Books Received Are Acknowledged under Heading: Books Received. This must be regarded as a sufficient return for the courtesy of the sender. Selections will be made for review in the interests of our readers as space permits.

Die normale Entwicklung des Knochensystems im Röntgenbild. (Radiologische Praktika, Band XV.) Von Dr. E. Ruckensteiner, Assistent am Röntgeninstitut des Rudolfinerhauses, Vorstand Reg.-Rat Primarius Dr. W. Frhr. v. Wieser, Wien. Cloth. Price, M. 18.60. Pp. 79, with 63 illustrations, 11 curves and 3 tables. Leipzig: Georg Thieme, 1931.

No system of Practical Radiology would be complete without a volume on the development of the bones and joints. In Volume XV of this series Dr. Ruckensteiner deals with this important phase of the work and does it in a very concise and satisfactory manner. He has delved extensively into the literature on the subject as the list of 353 references would indicate.

The illustrations are, for the most part, schematic drawings, which would seem to be preferable to roentgenograms. For example, the author illustrates the twenty-seven accessory bones of the carpus by two drawings whereas a large number of roentgenographic studies would be needed to show them all.

A feature of the work likely to appeal to the scientific mind is the representation of the time of appearance of centers of ossification, closure of epiphyses and facts of dentition by means of graphs. The curves are large, printed in colored inks and are very suitable for detaching from the book for mounting and hanging on the laboratory wall. Separate charts are obtainable from the publishers. These charts show at a glance not only the usual time of appearance of a center of ossification but also the proportion of cases in which such appearance is early or late, as indicated by the sharpness of the curve. By this method the author avoids the dogmatic statement as to exact time of appearance or closure, which has been definitely and erroneously fixed by other writers.

E. W. Hall

Diagnosis in Joint Disease: A Clinical and Pathological Study of Arthritis. By Nathaniel Allison, M.D., F.A.C.S., Professor of Surgery, in charge of Division of Orthopedic Surgery, University of Chicago, etc., and Ralph K. Ghormley, M.D., Associate in Orthopedic Surgery, Mayo Clinic; Assistant Professor of Orthopedic Surgery, Mayo Foundation, Rochester, Minn., etc. Cloth. Price, $9.00. Pp. 196, with numerous illustrations, including several colored plates. New York: William Wood and Company, 1931.

This book, as explained by the authors in its subtitle, is a clinical and pathological study of arthritis. In addition, it is an excellent roentgenological study. It is a well printed book with clear illustrations. Each case history is accompanied by reproductions of gross specimens, photomicrographs and roentgenograms. The end-result of each case is given. Each chapter on the various types of arthritis is prefaced by a discussion of the type, its pathological and roentgenographic appearances and its clinical characteristics.

The authors state in their preface that the entire subject of arthritis can be made much less difficult provided the student starts with a desire to discover the actual cause of the disease and to observe the essential tissue changes. In order to carry this out they have asked three questions in studying the data collected from any given instance of arthritis: What is the etiological factor? What tissue of the joint is primarily affected? What is the character of the tissue change? In many cases all these questions are readily answered with accurate diagnosis and simple classification. In many other instances one or another of the questions is unanswerable but nevertheless they believe a proper classification based upon sound pathology can be made.

In their classification, arthritis is divided into two main groups of cases: first, those of known origin, and second, those of uncertain origin. These groups are further subdivided. In the first is included: (1) traumatic arthritis, further divided into synovitis, loose bodies and cartilages, sprains, etc.; (2) bacterial agents such as arthritis due to the tubercle bacillus, the gonococcus, the staphylococcus and other pyogenic organisms, dysenteric, syphilitic, and the arthritis caused by the influenza bacillus and that accompanying rheumatic heart dis-

ease; (3) arthropathies such as tabes dorsalis, syringomyelia, leprosy, etc.; (4) constitutional disturbances, gout, hysteria, hemophilia, intermittent hydroarthrosis and anaphylactic reactions. The group of uncertain origin is divided into proliferative, degenerative and unclassified arthritis.

Individual chapters are devoted to tuberculosis, traumatic arthritis, arthritis associated with loose body formation, pyogenic infection of joints, proliferative, and degenerative arthritis.

This is a book which should be read by every roentgenologist, not only because of the subject matter presented, but also because of its manner of presentation. It is informative and many previously held opinions may be subject to change after careful study of the text. For instance, the statement is made that much has been written to aid in the roentgen diagnosis of tuberculosis of bones and joints but unfortunately much of this has not been based on fact. Cases thought to be tuberculosis have not been so proved. Thus, in their experience of over 100 proved cases, destruction at the diaphyso-epiphyseal junction is not often seen except in late cases or in cases of diaphyseal or metaphyseal tuberculosis. Also, the old saying that tuberculosis causes enlargement and squaring of the epiphyses has been found by them to be misleading. The belief that tuberculosis of the joints is easily recognized is not well founded in fact, as can be shown easily in the possible errors in diagnosis in even a small series of cases.

In the diagnosis of pyogenic infection of joints emphasis is laid upon the fact that the roentgen ray is of little help in the diagnosis of a suppurative joint condition. These diagnoses should be made early, before the roentgenogram shows anything but a full joint capsule. Its most important function is in revealing obscure bone lesions which may be adjacent to a joint and cause symptoms of joint disturbance.

The chapter on arthritis associated with loose body formation includes a summary of the principal theories of the causation of osteochondritis dissecans. The roentgenogram in this condition presents a more typical appearance than in any other joint disease. The discussion of proliferative and degenerative arthritis is full and complete.

The experience of the authors, the book being based upon 289 cases of joint disease, gives weight to their conclusions. The form of presentation makes easy the comparison of roentgen with pathological findings. The discussions are concise and summarize with sufficient detail the study of arthritis to the present date. The introductory chapter on the normal joint structures, their physiology and chemistry, contains much useful information for the roentgenologist. The bibliography is ample. The book is of a size and shape that renders it easy to hold while reading. The print is large and clear. Altogether it is an attractive and usable volume. It should be included in the library of every roentgenologist.

R. S. Bromer

Cutaneous X-Ray and Radium Therapy. By Henry H. Hazen, A. M., M. D., Professor of Dermatology, Medical Department of Georgetown University; Professor of Dermatology, Medical Department of Howard University. Cloth. Price, $3.00. Pp. 166, with 28 illustrations. St. Louis: The C. V. Mosby Company, 1931.

This small book constitutes, as the author states in the preface, an attempt "to write a short, essentially practical book that will aid in the selection of cases for irradiation, give safe advice as to the technic and warn against the many pitfalls." It contains little information that is not covered in a more comprehensive manner in MacKee's book on the same subject. Doses are empirically prescribed in sixths, eighths and even three-eighths of a skin unit as in many other dermatological texts without any statistical or experimental evidence to justify such fine mathematical precision.

Numerous minor errors, possibly resulting from a lack of proof reading, tend to mar the accuracy of the book. For instance, the statement is made that there is but little difference in the filtering power of steel and platinum in radium needles; radon is called "radium element"; the diameter of gold seeds is given as 0.3 mm.; and a therapeutic exposure of the face to roentgen rays is referred to as a "radiograph."

The first sixty-four pages deal with apparatus and technique. All doses are figured by the factor method and no mention is made of the international "r". A chapter is devoted to the action of radiation upon tissue and the last sixty-eight pages give brief descriptions of how the various dermatoses are treated. Few statistics and no photographs showing results are included.

The most valuable part of the book consists of a warning against the average dermatologist's sense of security in the use of repeated small doses of roentgen rays. Although Kingery's work on the cumulative action of radiation is not referred to, special emphasis is placed on the ill effects resulting from the summation of multiple small doses.

The author in the midst of his treatise on radiology regrets the fact that the average roentgenologist attempts to treat skin diseases. This is followed by a section on irradiation of cancer of the skin, lip and mouth which strikes a pessimistic note entirely at variance with the results obtained in good radiotherapeutic centers. Since the dose of roentgen rays recommended for squamous cell carcinoma is two to three skin units unfiltered over the primary lesion, and one skin unit through 3 mm. of aluminum over the metastatic glands, one can easily understand the author's lack of enthusiasm for irradiation No reference is made to the excellent results obtained in European clinics from the use of small platinum radium element needles in malignancies of the mouth nor to the massive dose technique used in this country in treating squamous cell carcinoma in all locations.

The book is recommended to those who want a brief survey of the field of radiation therapy in dermatology.

CHARLES L. MARTIN

Books Received

NORMALE UND PATHOLOGISCHE FUNKTIONEN DER VERDAUUNGSORGANE IM RÖNTGENBILD. Von Dr. Rudolf Becker, Röntgeninstitut des Theresienkrankenhauses, Mannheim, and Dr. Albert Oppenheimer, Röntgenabteilung der Med. Universitäts-Poliklinik, Frankfurt a. M. Paper, price, M. 16.75; bound, M. 18.75. Pp. 144, with 255 illustrations. Leipzig: Georg Thieme, 1931.

RÖNTGENUNTERSUCHUNGEN AM INNENRELIEF DES VERDAUUNGSKANALS. Ein Beitrag zur klinischen Röntgendiagnostik insbesondere von Entzündung, Geschwür und Krebs. Von Professor Dr. Hans Henrich Berg, Chefarzt der medizinischen Klinik der städtischen Krankenanstalten in Dortmund. Second, enlarged edition. Paper, price, M. 30; bound, M. 32. Pp. 248, with 247 illustrations. Leipzig: Georg Thieme, 1931.

ZEHN JAHRE FORSCHUNG AUF DEM PHYSIKALISCH-MEDIZINISCHEN GRENZGEBIET. Bericht des Institutes für physikalische Grundlagen der Medizin an der Universität Frankfurt am Main. Herausgegeben von o. ö. Prof. Dr. Friedrich Dessauer, Direktor des Institutes. Cloth. Pp. 403, with 190 illustrations and one colored plate. Leipzig: Georg Thieme, 1931.

LEHRBUCH DER RÖNTGENSTEREOSKOPIE. Von Dr. Max Cohn, Dirig. Arzt der Röntgen-Abt. am Städt. Krankenhaus im Friedrichshain, Berlin, and Dr. Walther Barth, Physiker der I. G. Farbenindustrie Aktiengesellschaft (Agfa-Filmfabrik). Paper, price, M. 30; bound, M. 33. Pp. 323, with 193 illustrations. Leipzig: Georg Thieme, 1931.

STUDIES IN THE PHOTO-ACTIVITY AND THERAPY OF THE TUNGSTEN-TITANIUM ARC. By J. Burdon-Cooper, M.D., B.S., B.Sc. (Durh.), F.R.C.S.E., D.O. (Oxon.), F.C.S., Late Lecturer Physiological Optics, Department of Ophthalmology, University of Oxford: Doyne Lecturer and Medal, Oxford Ophthalmological Congress, etc., and Arthur Roberts, T.D., F.R.C.S.E., M.R.C.S. Eng., Major R.A.M.C. (Ret.); Consulting Aural Surgeon, etc. Cloth. Price $3.50. Pp. 85, with illustrations. New York: William Wood and Company, 1931.

CUTANEOUS X-RAY AND RADIUM THERAPY. By Henry H. Hazen, A.M., M.D., Professor of Dermatology, Medical Department of Georgetown University; Professor of Dermatology, Medical Department of Howard University. Cloth. Price, $3.00. Pp. 166, with 28 illustrations. St. Louis: C. V. Mosby Co., 1931.

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ABSTRACTS OF ROENTGEN AND RADIUM LITERATURE

ROENTGEN AND RADIUM THERAPY

Murdoch, J. Contribution à l'étude de la dosimétrie en curithérapie. (Dosimetry in radium therapy.) *Acta radiol.*, Sept. 30, 1930, *11*, 350–397.

This is a description of an ionometric chamber with liquid contents with a volume of 2 cubic millimeters by means of which the gamma rays in the immediate vicinity of radium tubes and needles can be measured. The combined use of ionometric and energetic measurements led to the adoption of the erg-cubic centimeter as the absolute dosimetric unit in radium therapy. The author describes the mapping out of curves of isodoses for radium apparatus. Clinical applications of the method are described and the determination in erg-cubic centimeters of the amount of energy absorbed by the tissues.

There is also a description of a method which allows a rational distribution of radium tubes on surface mass so as to ensure homogeneous distribution of radiation on flat and curved surfaces. A few simple appliances often used in practice are described. The determination of the value of the erythema dose in erg-cubic centimeters is described and a study made of the various skin reactions resulting from radiations of varying intensity expressed in erg-cubic centimeter. An analysis is given of a few clinical cases treated by means of moulded apparatus with irradiation schemes established according to this method, and a study of the biological reactions seen in the various tissues after applying varying amounts of energy during the course of the radium treatments.—*Audrey G. Morgan.*

Pausdorf, Hans, and Nell, W. Die Blutdruckschwankungen nach Röntgenbestrahlungen und ihre klinische Bedeutung. (Blood pressure variations after roentgen irradiation and their clinical significance.) *Strahlentherapie*, Sept. 27, 1930, *38*, 40–53.

The blood pressure variations that follow a roentgen irradiation immediately are not due to the same cause as the fall of blood pressure that occurs after twenty-four to forty-eight hours. While the former are irregular and do not follow any law, the latter show a wave-like course, and after intensive irradiation may reappear after twenty-five to thirty-five days and again after fifty to seventy days. This fall of blood pressure is not caused by the action of the roentgen rays on the suprarenals, but is a manifestation of a general reaction caused by intense destruction of cells and the increased irritability of the vasodilating system caused by the roentgen irradiation; the effects of vessel dilatation and cell destruction supplement each other. As a manifestation of a general reaction this fall of blood pressure is important in diagnosis and in determining general treatment and the time for repeating the irradiation.—*Audrey G. Morgan.*

Schultze, Gunter K. F. Die Stickstoffausscheidung im Harn nach Röntgen- und Radiumbestrahlung. (Nitrogen excretion in the urine after roentgen and radium irradiation.) *Strahlentherapie*, Sept. 2, 1930, *37*, 642–658.

The literature is reviewed and the author's own experiments in determining nitrogen excretion after roentgen and radium irradiation reported. His work shows that the commonly accepted belief that roentgen irradiation does not cause increased nitrogen excretion is not true. It should be remembered however that patients are never really normal individuals and that the diseases treated may have varying effects on nitrogen excretion so the results cannot be interpreted uniformly. But it is certain that with large doses there is breaking down of albumin with increased nitrogen excretion. This is shown by animal experiment also; but even with the usual therapeutic doses there may be increased nitrogen excretion. The author's cases were all carcinoma of the cervix and in about half the cases there was a very marked increase of nitrogen excretion. The reaction was much stronger and more constant when the roentgen irradiation was preceded by radium irradiation. It is possible that in the cases in which no increase of nitrogen excretion was observed there was a small amount of increase over a protracted period not shown in the tests made. There was increased nitrogen excretion

after radium irradiation in all cases. It was more intense and more constant than after roentgen irradiation. While other authors report an increase of creatinin nitrogen the author's experiments did not show that creatinin nitrogen was involved in the increased total nitrogen excretion.

So far the increased nitrogen excretion cannot be used in prognosis or as evidence of biological dosage, as it is inconstant and not enough is known about the effect on it of different diseases, technique of irradiation and dosage.—*Audrey G. Morgan.*

DUHEM, P. La physiothérapie dans le traitement de la poliomyélite. (Physiotherapy in the treatment of poliomyelitis.) *Presse méd.*, Mar. 18, 1931, *39*, 400–403.

Since 1919 the author has treated more than 800 cases of chronic poliomyelitis. In 250 cases a comparative study of the value of roentgen therapy and physiotherapy was made, 150 being treated by a combination of roentgen and physiotherapy and 100 by physiotherapy alone. It was found that all cases without reaction of degeneration became well regardless of whether the combined method or physiotherapy alone was used. In the more advanced cases, with total reaction of degeneration, the percentage of permanent cures was slightly larger with physiotherapy alone.

The conclusion is reached that roentgen therapy does not contribute to the improvement of the results in the chronic forms of poliomyelitis. The various methods of physiotherapy (local balneotherapy, diathermy, electro therapy, etc.) are discussed in detail.—*T. Leucutia.*

MISCELLANEOUS

HOLZKNECHT, GUIDO. Die innere Entwicklung der Röntgenologie in Österreich. (The development of roentgenology in Austria.) *Strahlentherapie*, 1930, *36*, 403–409.

There are two periods in the development of roentgenology: in the first, the rays were used for the diagnosis of fractures and foreign bodies, in the second, diagnosis was extended to pathologic conditions of all organs and roentgen treatment of tumors and inflammations developed. In the first period technique was difficult and diagnosis easy; during the second, diagnosis became constantly harder and technique easier. Now any physician can learn the technique in six months but diagnosis has become so difficult that it is almost impossible. It is surprising that results in widely separate parts of the world agree as well as they do.

Twenty years ago the author and his friend Kienböck decided that technique could safely be left to the technician and physicists but that diagnosis and therapy remained tremendous tasks that could be handled only by the physician. It became necessary for roentgenologists to specialize and as knowledge broadened to specialize still further. If a science is fixed and stable an individual can learn it in a few years, but in a new science that is developing with enormous rapidity one person can only master a small special field. Some special fields that have already been developed are: diagnosis of the skull, which includes diseases of the eyes, ears, nose and nervous diseases and is by far the most difficult field of diagnosis. Other fields are the teeth and jews, the esophagus, heart and blood vessels, the rest of the mediastinum and tumors of the thorax, tuberculosis and other lung diseases, the stomach and intestines, the female genital organs, the bones and joints. Treatment covers the field of tumors, inflammations, trophic-dyscrasic and endocrine diseases.

The second great need was the establishment of a fundamental knowledge of roentgen physics, roentgen anatomy and physiology, roentgen biology and general roentgen diagnosis and therapy and the establishment of roentgenology as an essential part of medicine. In addition to this the specialist must communicate his knowledge to others so that what he learns and what he adds that is new can be carried on by others. The natural place for teaching roentgenology seems to be the roentgen institutes of hospitals. The universities are not adapted for the purpose because they are bound by tradition and only adapt themselves slowly to new things.

Many physicians thought that roentgenology should simply be absorbed in the medical specialties, that each specialist should take over the part of roentgenology belonging to his field But that was found to be quite impossible and the roentgen specialities divided along quite different lines. The lines of division of roentgenology in some cases ran transversely through the medical specialties and in some cases combined small special fields in medicine. Possibly greater simplification will be possible in the future.—*Audrey G. Morgan.*

Chamberlain, W. E. Radiology as a medical specialty. *Radiology*, 1929, *13*, 229–233.

Chamberlain believes that the problem of lay laboratories will not disappear until the medical profession recognizes that radiology is truly a branch of medicine, and that it is fundamentally wrong to send patients to lay laboratories. There will not be a satisfactory influx of young medical graduates into radiology, nor a satisfactory development of radiology in the hospitals, until the relations between hospitals and radiologists have been improved. The hospital radiologist must be offered an opportunity for self-development comparable with that of his brothers in medicine and surgery. Under the present scheme of things there are many instances of the exploitation of radiologists by hospitals. The amassing of profits by the hospital from the radiologist's services constitutes exploitation whenever such profits exceed what can be justified by the material outlay and investment in apparatus and space. There is need for a revision in the fee schedules for radiologic services, because most of those now in operation place the radiologists in the position of selling celluloid by the square inch instead of rendering a type of medical consultation service.—*J. D. Camp.*

Barker, Walter C. Investigation of the characteristics of the Philips type of Müller Metalix tubes as revealed by the roentgenogram. *Radiology*, 1929, *13*, 283–292.

The purpose of the investigation was to determine the class of work in which the Philips type of Müller Metalix tubes will produce better roentgenograms than the Coolidge tubes. For the investigation two Müller Metalix tubes of the Philips type and five Coolidge tubes were used, the focal spot being measured by the pinhole method: (1) 3 kw Metalix Radiator, focal spot 3.5×3.5 mm.; (2) 6 kw. Metalix Watercooled, focal spot 3.5×3.75 mm.; (3) 10 milliamperes Coolidge, focal spot 3×3 mm.; (4) 10 milliamperes Coolidge, focal spot 4×4 mm.; (5) 30 milliamperes Coolidge, focal spot 4.75×5 mm.; (6) 100 milliamperes Coolidge, focal spot 8×8.5 mm.; (7) B.F. Universal, focal spot 7.5×11 mm. The energy for the tubes was supplied by a double cross arm rectifying switch type of machine, with all exposure factors controlled and carefully checked. To analyze the detail of structure, wire mesh was used. The distances that the mesh was raised from the films were chosen to represent the structures of the body usually examined. It was thought that the study of the wire mesh 2 inches away from the film would correspond to the extremity group; 6 inches away from the film, to the pelvic structures; 8 inches away from the film, to the structures in the chest, and to have an equivalent for various intermediate structures of the body, the wire mesh was examined 4 inches away from the film. Wire mesh of half-inch squares seemed to be best for the study of the characteristics produced by the focal spot, but as the structures of the body are more compact, it was thought that a finer wire screen might improve the visibility, so a series of films was made of one-quarter inch square wire mesh. The diameter of the wire forming the screen of the half-inch mesh was approximately 1 mm. and that of the quarter-inch square mesh was approximately 0.5 mm. Films (14×17 inches) were exposed over their entire surfaces, and to eliminate the possibility of poor contact no screens were used.

It was the conclusion of the author that the construction of the Philips type of Müller Metalix tube, by the elongation of the focal spot to carry larger amounts of energy, and the geometry, to compensate for the rectangular shape of the focal spots, make the tubes unsatisfactory where detail is important over a large area, as in the examination of the bony pelvis. For this class of work much better films are obtainable by using the Coolidge tube, and, as speed in exposure time is not usually necessary, the finest focal spot Coolidge tube may be used, and this gives much sharper detail of structure than the 3 kw. radiator type Philips tube. Where small areas were examined, there was no difference in detail on the films, whether made by the Coolidge or Philips tubes, and the speed of exposures, as recorded in the tables given in the paper, is rapid enough to meet the usual requirements. Therefore, no advantage was gained by using the Philips tube.—*J. D. Camp.*

Behnken, Hermannm and Jaeger, Robert. Die Reproduzierbarkeit der Röntgendosiseinheit. (Bemerkung zu der Arbeit von A. Reisner und Th. C. Neeff: "Hauttoleranzdosis und Strahlenqualität.") (The reproducibility of the roentgen dose unit. Remarks on the paper of A. Reisner, and Th. C. Neeff—"Skin tolerance dose and radiation quality.") *Strahlentherapie*, 1930, *36*, 778–785.

In a series of comparative measurements on the accuracy of the roentgen dose unit "r," as used in various roentgen institutes, Reisner and Neeff found variations between various r-units which amounted to as much as 20 per cent. Behnken and Jaeger, the physicists of the German Reichsanstalt, discuss the possibilities for variations in r-units of different instruments and come to the conclusion that at the present time the largest difference is only a few per cent and the average of a number of measurements on various instruments is taken to only 1 per cent. They conclude from their work that considerable errors may creep into the accuracy of the determination of the r-unit if the measuring arrangement for the comparison of the intensities in the large standard chamber and the small chamber is not carefully selected. They also conclude that at the present time measuring instruments can very well be calibrated in the r-unit and that this unit can be safely transported from one place to the other if proper precautions in calibration and transportation are taken.—*Otto Glasser.*

BJÖRLING, E. Eine biologische Einheit bei Dosierung der Röntgenstrahlen. (A biological dosage unit for roentgen rays.) *Strahlentherapie*, 1930, *36*, 751–777.

The author suggests supplementing the international physical definition of the r-unit by a biological measuring system and introduces the "bio-r," which he defines as that roentgen dose which for the normal radiation quality, produces the biological effect of one r. In order to arrive at some conclusion as to the value of the "bio-r," he uses Jüngling's method of germinating beans in the determination of radiation intensities. After modification of this method, it is possible to graduate the biological effects rather accurately. The observations on a large series of beans was correlated to the intensities measured in r-units. These r-units were gained by means of a method worked out by the author whereby luminescence of tungsten under the influence of various qualities and quantities of roentgen rays was determined optically in Hefner-meter units. The Hefner-meter units were directly transferred into r-units. In order to obtain reliable measurements for the various radiation qualities, the amount of rays transmitted through 1 mm. of copper was determined. The radiation quality then can be expressed in numbers whereby the transmission of 50 per cent, which would correspond to one-half value of 1 mm. in Cu, is taken as the standard.

With these exact dosage factors as a basis, the biological effects of different radiation beams upon the beans were correlated with doses in r-units and the results collected in a series of curves. These relations which permit expressing all the biological doses in "bio-r" show that for the same quantity of radiation as measured in "r" the soft rays have a considerably greater biological effect than the hard rays.—*Otto Glasser.*

GFRÖRER, O. Ueber die Eichung von Grenzstrahlröhren. (The calibration of Grenz-ray tubes.) *Strahlentherapie*, 1930, *36*, 786–804.

The author gives a description of the various methods of calibration of roentgen tubes for the production of very soft roentgen rays, or so-called Grenz rays. In studying the influence of the fluctuations of the line upon the efficiency of the apparatus, he comes to the conclusion that these fluctuations influence the whole treatment technique with Grenz rays to a much larger extent than when using roentgen rays. He suggests eliminating these fluctuations by an automatic stabilizer, or by constant control and regulation of the voltage and current during the treatment. Examination of the accuracy of the voltage measurement by a primary voltmeter shows that this method is not very accurate. Sphere gap measurements with the use of a rectifier tube and an electrostatic electrometer are suggested for determination of the secondary voltage. The values obtained for various conditions agree well with those of other authors, for instance, with those of Glasser and Bucky. The intensities were determined in r-units by means of the Küstner apparatus with a small Grenz-ray chamber. The intensities which were determined for various treatment techniques are given in their dependence upon the voltage, the current and the distance. The output of several commercial apparatus was also determined, and it was found that for the same voltage and same tension the radiation intensity was practically the same for all apparatus. For the practical use of these various dosage factors in the therapy department a special system is proposed whereby the intensity and secondary voltage is noted from time to time on a standardization chart which permits the continuous control of the efficiency of the Grenz-ray tube.—*Otto Glasser.*

Knipping, P. Bemerkung zu meinem Artikel: 'Ueber Physik und Technik der Kathodenstrahlen." (Remarks on the article on "Physics and technique of cathode rays.") *Strahlentherapie*, 1930, *36*, 808.

This refers to an early article on the physical effects of cathode rays. The author shows that the Dessauer point heat theory belongs to his second group of explanations for the biological effect of cathode rays, namely, the study of the increase in temperature through high speed electrons.—*Otto Glasser.*

Glocker, R. Die Bedeutung der Röntgenstrahlen für Wissenschaft und Technik. (The significance of roentgen rays in science and technique.) *Strahlentherapie*, 1930, *36*, 660–670.

Glocker, well-known director of the Roentgen Institute of the Technical High School in Stuttgart, gives a detailed account of the practical use of roentgen rays in the investigation of faulty materials, and of the various spectrometric methods of investigating the structure of matter and the changes in certain materials by temperature, pressure, etc. The spectrometric methods used for this purpose are described, and a series of pictures obtained by these methods is shown.—*Otto Glasser.*

Nikitin, S. A. Untersuchungen über Röntgensensibilisierung. III. Ueber die sensibilisierende Wirkung des Thoriumnitrats. (Investigations of sensitization by means of roentgen rays. III. On the sensitization effect of thorium nitrate.) *Strahlentherapie*, 1930, *36*, 745–750

Various pathological changes of the skin of mice, rats and guinea pigs were observed after the sub- and intracutaneous injection of 10 per cent thorium nitrate. A study of the combined application of thorium nitrate and roentgen rays (230 kv.; 0.5 mm. Cu and 1 mm. Al; 3.5 ma.; 25 cm. focal distance) showed that the biological effect was qualitatively the same as produced by thorium nitrate alone, and that it made no difference whether the thorium nitrate was applied first and then the roentgen rays, or vice versa. This observation excludes the theory that the increased effect of this combination does not depend upon an increased emission of secondary electrons of the thorium under the influence of the roentgen rays, as has been suggested by Ellinger, Gans and Berg. It seems that the roentgen rays prevent the resorption of the thorium nitrate, thus not interfering with its biological action.—*Otto Glasser.*

Menville, L. J., Ané, J. N. and Blackberg, S. N. A comparative x-ray study of passage of foodstuffs through gastro-intestinal tract of rats. *Proc. Soc. Exper. Biol. & Med.*, April, 1930, *27*, 641–645.

A study was made of the passage of carbohydrates, protein and fatty foodstuffs through the gastrointestinal tract of rats. Thirty-nine animals were used; and they were fasted for forty-eight hours and deprived of water for twenty-four hours before examination. The various foodstuffs ingested were approximately of the same general consistency.

The first fluoroscopic observations were made immediately after the feeding, and in every instance the stomach was found filled and some of the food had already passed through the pylorus. Careful examinations were then made every fifteen minutes until the food column was visualized in the cecum, and the stomach and small intestine were found empty.

The average emptying time of the stomach when carbohydrate was fed was the most rapid, the protein diets were next, and the fat was the slowest of all. The cecum appearance time of the food column of the protein-fed group was the fastest, next the carbohydrate and last the fat group. The small intestine emptying time of the carbohydrate group was the fastest, next the protein and last the fats. The colon emptying time of the carbohydrate group was the fastest of all and there was only slight difference between the protein and fat groups. The observations of the colon are not as accurate as those of the stomach and small intestine because this organ empties very slowly, and for this reason the fluoroscopic examinations were of longer intervals.

The rate of emptying time of the stomach, small intestine and colon corresponds closely to those found by other observers. Although the emptying times observed were approximately the same as those of previous workers, marked differences were noted for the rates of passage of the various food stuffs in the present experiments as compared with others. The passage of protein through the small intestine of rats is much faster in every instance than fat and only slightly faster than carbohydrate. This is at variance with the findings of the

earlier investigators who stated that proteins passed through the small intestine slowly, fats a little faster and carbohydrates fastest of all.—*B. Cohen.*

KEITH, W. S., and BRIGGS, D. R. Roentgen ray visualization of spleen following injection of emulsions of halogenated oils. *Proc. Soc. Exper. Biol. & Med*, March, 1930, *27*, 538–540

In view of the well-known phagocytic properties of the cells of the reticulo-endothelial system for finely divided foreign materials injected in the blood, an attempt was made to visualize organs containing those cells by injecting particulate matter which was relatively opaque to roentgen rays Lipoidol emulsified in gum acacia was used Doses varying from 0.5 to 4 c.c. of oil per kilo body weight were injected into a tail vein of 7 white rats. Four receiving smaller amounts survived indefinitely. In certain experiments there was used a gum acacia-water emulsion of the brominated esters of olive oil. Of this material 0.5 to 3 c.c. per kilo body weight was injected into 11 rats, all of which survived.

The minimum amounts for visualization of the spleen in the rat would appear to be about 1 c.c. oil per kilo body weight. The shadow reaches maximum intensity about one-half hour after injection. The shadow fades and disappears entirely in about one week. The liver shadow is slightly intensified following the injection.

A few similar experiments have been done on dogs. The long strap-like spleen can be visualized after the injection of about 1.5 c.c. of oil per kilo body weight.—*B. Cohen.*

JORSTAD, LOUIS H. Some observations on vitamins A and D; activation of yeast by x-ray and other radiation. *Proc. Soc. Exper. Biol. & Med.*, June, 1930, *27*, 930–932.

The experiments were done on compressed brewer's yeast. When exposed for periods of five to sixty minutes to a Cooper-Hewitt lamp the yeast protected somewhat against rickets if the exposure was for 30 minutes, but complete protection was not afforded with specimens irradiated for less than 50 minutes. The 60-minute irradiated yeast was not as protective as the 50-minute. Yeast exposed for 30 minutes did not protect against vitamin A deficiency; an exposure of at least 50 minutes was required to yield material giving full protection. With a quartz light complete protection against xerophthalmia and rickets occurred after irradiation of the yeast for 5 to 7 minutes. In each case 5 per cent by weight of yeast was added to the standard rations. The irradiation with roentgen rays was made with the following setup: 10 inch distance, 9 inch spark gap, 90 kv., 4 minutes' exposure giving 20 ma-min. The yeast cake exposed was 1 cm. thick. Greatest protection against rickets was afforded by the 20 ma-min. exposure.

It is concluded that the Cooper-Hewitt lamp, quartz light and low voltage roentgen rays caused an activation of the vitamin D and vitamin A in yeast fed to rats maintained on deficient diets. The period of exposure in each case varies with the type of light used. There is a maximum point of activation for each light.—*B. Cohen.*

MENVILLE, LEON J., ANÉ, J. N., and BLACKBERG, S. N. A fluoroscopic study of the motility of gastrointestinal tract of rats fed a vitamin deficient diet. *Proc. Soc. Exper. Biol. & Med.*, June, 1930, *27*, 894–895.

A comparative study by means of frequent fluoroscopic observations was made of the motility of the gastrointestinal tracts of rats fed diets deficient in vitamin B, vitamin D and also a diet deficient in vitamins A and D with a balanced mineral content. Seventy rats were used; 27 served as controls. The animals were fasted for forty-eight hours and water was withheld for twenty-four hours before the start of the experiment, when they were fed a meal of 5 grams of barium sulfate and 5 cc. buttermilk. They were allowed to eat for 20 minutes and then immediately fluoroscoped in loose cotton bags to ascertain if their stomachs were full. Observations were repeated every fifteen minutes thereafter until the cecum appearance of the food column was observed, and continued until the small intestine emptied.

The fluoroscopic observations demonstrated that rats fed a diet deficient in vitamin B showed a marked hypomotility of their gastrointestinal tract. The same was found for vitamin D deficient rats but not so marked. The vitamin A-D deficient rats showed a motility comparable to the normal.—*B. Cohen.*

GOEHL, R. O., LYNCH, F. W., BORMAN C., and WANGENSTEIN, O. H. Evaluation of x-ray

evidence as a criterion of strangulation obstruction. *Proc. Soc. Exper. Biol. & Med.*, June, 1930, *27*, 952–954.

This study is an attempt to evaluate the significance of roentgen evidence in the early recognition of strangulation obstruction. Strangulation obstruction in dogs was established aseptically under local anesthesia (procaine) of the abdominal wall. About 24 inches of small intestine, together with its mesentery, was tied off about 18 inches above the ileocecal valve. An attempt was made to establish varying grades of strangulation but the experiments reported are concerned with two types: one in which the blood supply to the loop was arrested, and the other was strangulation in which a slight pulsation could be felt in the mesenteric loop beyond the ligature, immediate congestion and discoloration of the bowel being present. Perforated lead shot were sewed to the mesenteric border of the strangulated loop to determine whether the bowel proximal to the obstruction or the strangulated loop distended most readily.

It was found that gaseous shadows were observed in the small intestine fairly early during the course of the obstruction. Gaseous shadows were observed proximal to the obstruction in four to five hours after the establishment of the obstruction. Gas was first observed in the small intestine three hours after the establishment of strangulation obstruction and the longest interval was eight hours, the average being six hours.

The strangulated loop frequently did not exhibit gaseous distention in excess of that shown by the bowel proximal to the obstruction. During the latter course of the obstruction the distention of the strangulated segment could usually be traced with ease on the roentgen film. In several of the animals gaseous distention of the intestine distal to the obstructed loop was also observed. This is probably significant of the concomitant occurrence of inhibition ileus as seen in the paralytic ileus of peritonitis.

The results of this study indicate that the roentgen ray is not of the same value in detecting the presence of strangulation as it is in the early recognition of simple obstruction of the intestine.—*B. Cohen.*

Adams, W. E. Further studies in obstructive pulmonary atelectasis. *Proc. Soc. Exper. Biol. & Med.*, June, 1930, *27*, 982–983.

Artificial obstruction was used; this obstruction being located in the primary bronchus of the lung lobe. Either total or valvular obstruction in the presence of a straining type of respiration was followed by a massive atelectatic. condition of the obstructed lung. If a quiet, normal type of respiration was exhibited no resultant atelectasis was observed. It was found that cauterization of the bronchus was followed by a complete stenosis in from one to two weeks. If this stenosis was located in the primary bronchus of the lung lobe that lobe was found to be completely atelectatic with the secondary bronchi and bronchioles filled with a mucogelatinous material. If the stenosis was located in one of the several divisions of the primary bronchus of the lobe, no resultant atelectasis occurred.

In view of these experiments it appears very probable that there are communications between the smaller air passages, or more likely of the air sacs and cells of the many lobules of the lung lobe. It also appears that obstruction of the primary bronchus or all of its divisions is necessary for the production of massive atelectasis of the lung lobe. Although a straining type of respiration appeared essential in the production of this condition within twelve to twenty four hours, it does not appear to be essential for its production over a longer period of time.—*B. Cohen.*

Coldwater, K. B. Action of x rays on glutathione content and oxygen consumption of normal and regenerating planarians. *Proc. Soc. Exper. Biol. & Med.*, June, 1930, *17*, 1031–1033.

The glutathione content was determined in two species of Turbellarians, *Planaria agilis* and *Proctoyla fluviatilis*. The former species possesses a high capacity of regeneration and shows a high concentration of glutathione. The latter, which exhibits a low capacity for regeneration, shows a lower content. In normal worms the formative cells are found in the parenchyma, principally in the dorsal region. This area corresponds to that showing the highest content of glutathione.

Quantitative examinations of the glutathione content of normal, regenerating and irradiated specimens of *Planaria agilis* were made by colorimetric estimations and by the Tunncliffe method. The glutathione content was found to decrease after irradiation with heavy ex-

posures of roentgen rays (approximately 2,000 R).

The oxygen consumption of individual specimens of *Planaria agilis* was determined by the Winkler method. Oxygen consumption remains about normal during regeneration. Oxygen consumption of both normal and regenerating worms is markedly decreased by heavy exposures to roentgen rays.

In view of the stimulating action of glutathione upon cell division and the high concentration of this compound in embryonic cells the destruction of glutathione by roentgen rays or at least its inactivation offers an explanation of the selective action of roentgen rays upon cells undergoing mitotic division and upon embryonic cells of planarians and other forms.—*B. Cohen.*

PHEMISTER, D. B. Repair of bone in the presence of aseptic necrosis resulting from fractures, transplantations, and vascular obstruction. *J. Bone & Joint Surg.*, Oct., 1930, *12*, 769–787.

Aseptic necrosis of bone may result from a number of causes, such as vascular disturbances, injuries, the action of chemicals, and the application of radium in malignant disease. The process of repair of the damaged area differs with the amount of functional stimulation to which the part is subjected during the reparative period and with the nature of the causative agent. It also differs from that seen in the case of necrosis produced by infection. Necrosis en masse produced by severe infection is nearly always followed by a fibroblastic and fixed tissue phagocytic reaction which usually results in complete absorption of the dead bone if the area is small, or in sequestration, if it is large. However, mild inflammatory reactions, particularly when associated with embolic or thrombotic processes and due to low grade microorganisms, may sometimes result in necrosis which is followed by simultaneous absorption of dead bone and incomplete, irregular replacement by new bone. This same change may be observed in a bone graft when mild infection has occurred. Epiphysitis may result in rather extensive necrosis which is followed by absorption and a certain amount of collapse and new bone formation with eventual bony reconstruction of a deformed epiphysis.

The introduction of radium into or in contact with bone in the treatment of malignant disease may lead to more or less extensive bone necrosis without destruction of the peripheral layer of the overlying soft parts, in which case the necrotic bone remains free from infection. The necrotic bone produced in this way may be sequestrated at a very slow rate or, if it performs a supporting function, it may be very slowly absorbed and replaced by new bone. If infection is present, it is always slowly sequestrated. The explanation of the slow absorption is to be found in the fact that the tissues adjacent to the dead bone are radium burnt and consequently bring about repair very slowly. In experimental radium necrosis in the dog the dead bone was very slowly replaced but its fate was dependent to a considerable extent on the amount of function which the limb performed. If no fracture occurred there was gradual substitution of new bone, but if a fracture occurred with consequent disuse, there was gradual sequestration of the dead bone in the course of one or two years.

The fate of bone which undergoes aseptic necrosis as a result of circulatory disturbance varies considerably, according to the environment of the necrotic area. If the necrotic bone is attached to and directly continuous with living bone, by a process of creeping substitution, the old bone is gradually absorbed and replaced by new bone so that in the course of months or occasionally years, the necrotic area is more or less completely transformed into a living one. Whether the amount of new bone formed is as great as the amount of bone that died, depends largely on the extent of living bone with which it is in contact and the amount of osteogenic elements surviving about its periphery. In regard to function, the greater the degree of function, the greater the rate and degree of transformation into new bone. Chances for regeneration and transformation into new bone are greatly lessened if the necrotic bone is largely or wholly intra-articular and extensively bordered by articular cartilage. Thus, injury to vessels may be the cause of some of the cases of Kienböck's malacia of the carpal lunatum and of Legg-Perthes' disease,—as when it follows reduction of congenital dislocation of the hip. Operations which involve severance of bone or extensive separation of soft parts from bone may occasionally interfere with the blood supply sufficiently to cause massive necrosis. A case of this sort, an arthroplasty of the hip is reported with roentgenograms showing such ne-

crosis. Extensive separation of periosteum from bone, particularly during the growing period with resultant injury of nutrient and metaphyseal vessels may result in extensive aseptic necrosis of bone. Such bone necrosis is no doubt occasionally produced by extensively denuding operations.

Fracture may cause necrosis by interference with the blood supply of the bone in the immediate vicinity of the break or by damage to larger vessels that furnish a large part or all of the nutrition to one of the fragments. It may also occur in fractures bordering on joints from injury to the blood vessels to a large part or all of the joint fragments. It undergoes either partial or total necrosis. Thus necrosis of the proximal fragment occurs in a not inconsiderable percentage of cases of complete intracapsular fracture of the neck of the femur. At the end of the period of immobilization the distal living fragment usually shows roentgen signs of atrophy due to disuse, but the necrotic head which cannot atrophy casts practically as even and heavy a shadow as at the time of fracture. This usually makes it possible to diagnose necrosis roentgenologically at this stage. In cases of non-union the head of the femur casts a shadow for at least one to two years which is denser than that of the neighboring living bone which is atrophic from disuse. One such case is illustrated by roentgenograms. In fracture of the neck of the astragalus the body may rarely have so much of its blood supply cut off that it undergoes extensive necrosis. The roentgen signs of necrosis in such a case are similar to those of fracture of the neck of the femur.

Nearly all the more recent studies tend to confirm the view that when bone is transplanted the bone cells within the lacunae practically all become necrotic as a result of cutting off of the circulation. The unossified osteogenic elements along the periphery and in the vascular canals may survive. The extent to which they proliferate and take part in the transformation of the necrotic bone depends to a considerable extent upon the location of the transplant and the extent to which it is subjected to functional stimulation. If the transplant is in the course of the bone, with the fragments of which it should be united in order that the continuity of the bone be restored, and as a part of which it should function, the surviving osteogenic elements proliferate and take an active part in osteosynthesis and transformation of the necrotic portion of the graft. In case a bone graft of the whole thickness is transplanted into a defect in a bone and anchored by insertion of one end into the medullary cavity, the subsequent changes in the intramedullary and extramedullary portions are different, due to some extent to their differences in function.

The role of embolism in the production of both septic and aseptic bone necrosis is still imperfectly understood. Aseptic bone necrosis, the result of proved thrombosis or embolism, is a condition that has rarely been reported in man. It has been produced experimentally by injection of small aseptic emboli into the femoral artery. Phemister discusses the subject of embolism and thrombosis as a cause of aseptic necrosis in such detail that it is impossible to give the various experimental data in abstract form. This entire paper should be read by roentgenologists, and especially by those who work in conjunction with surgeons performing bone surgery.—*R. S. Bromer.*

Benner, Sven. Über die Schwächung der Radiumstrahlen durch die Wände und die Fussboden in Gebäuden. (The weakening of radium rays by the walls and floors of buildings.) *Acta radiol.*, Aug. 15, 1930, *11*, 310–320.

By means of an ionization instrument previously described in *Acta radiol.*, the intensity of radiation in a room adjoining one used for distance treatment with large quantities of radium has been determined. The absorption in walls and floor was computed and it was found that the secondary radiation from these, although considerable, does not change the order of magnitude of the intensity of radiation within the 6 to 8 meters nearest to the radium.

On account of the great penetrating power of the rays it is suggested, in analogy with the requirements for hard roentgen rays (tolerance dose in 20,000 hours at a skin unit dose of about 600 r) that in premises where the same persons have to remain for hours daily for a number of years the maximum intensity permissible should not exceed 5.10^{-4} r per minute, at which rate it would take 60,000 hours, about seven years, to reach a skin unit dose or 2000 r. An intensity in excess of this maximum was found in very few spots in the premises examined.

As a rule, protective lead screens cannot be used except on the floor underneath the distance treatment apparatus. When new build-

ings are erected, however, the walls of rooms intended for such purposes should be built of bricks or barite plates and barite filling should be used in floors and ceiling.—*Audrey G. Morgan.*

SIEVERT, ROLF M., and THORAEUS, ROBERT. Experimental measurements of the lead-equivalence of various building-materials. *Acta radiol.*, Aug. 15, 1930, *11*, 331–345.

The absorption of some building materials has been compared with that of lead by means of an ionization method. Some sources of error, liable to occur under certain circumstances in photographic methods of determining the protective power, are briefly discussed.

Investigations have been made of a number of different materials at five different voltages, 75, 100, 125, 150 and 175 kv., and with several thicknesses of the layers of material. The results, together with earlier observations at the Physical Laboratory of Radiumhemmet, have been collected in a table in which figures obtained by Kaye and Owen, Berthold, and Berthold and Glocker are also given. The table, being intended for practical use, gives the thickness of the materials corresponding to 2 mm. of lead at diagnostic voltages (75 to 125 kv.) and to 4 mm. lead at therapeutic voltages (150 to 175 kv.), which protection meets the requirements of the International regulations passed at the Second International Congress of Radiology at Stockholm in 1928. The figures obtained by the different authors do not always agree very well, which is probably due partly to differences in the methods of experiment.—*Audrey G. Morgan.*

VAN DER TUUK, J. H., and BOLDINGH, W. HONDIUS. Die Bleischutzdicken in den deutschen Strahlenschutzvorschriften. (The thicknesses of the protective lead in the German radiation protection rules.) *Fortschr. a. d. Geb. d. Röntgenstrahlen*, June, 1930, *41*, 965–967.

As is known, the German Roentgen Society, following the recommendations of Glocker and Reuss, has adopted protective lead values which are different from those recommended by the International Congress of Radiology in Stockholm. This difference is chiefly between 100 and 200 kv. Thus while the International Congress recommends four different values (2.0 mm. lead from 100–125 kv., 2.5 mm. lead from 125–150 kv., 3 mm. lead from 150–175 kv., and 4 mm. lead from 175–200 kv.), the German Roentgen Society used only three: 2 mm. lead up to 125 kv., 3 mm. lead from 125–190 kv., and 5 mm. lead from 190–225 kv. The authors, in making elaborate measurements, found that the recommendations of the International Congress are more accurate.

The basis for the changes adopted by the German Roentgen Society is that the absorption coefficient of lead remains practically constant between 100 and 200 kv. While this is admitted by van der Tuuk and Boldingh, it is emphasized that the measurements must actually be carried out behind lead walls and the values obtained as such be taken into consideration rather than the theoretical calculation of the lead absorption coefficient. It is impossible to admit, for example, that while a thickness of 3 mm. lead would give a sufficient protection for 189 kv., 190 kv. would at once necessitate a protection of 5 mm. lead. For this reason the rules of the International Congress are recommended in preference to those of the German Roentgen Society.—*T. Leucutia.*

GLOCKER, R. Zur Frage der "Bleischutzdicken" in den internationalen und in den deutschen Strahlenschutzvorschriften. (On the question of the lead protective thicknesses in the International and in the German radiation protection rules.) *Fortschr. a. d. Geb. d. Röntgenstrahlen*, June, 1930, *41*, 967–971.

In answer to the critical study of van der Tuuk and Boldingh on the accuracy of the German radiation protection rules concerning the lead thickness values between 100 and 200 kv., the author states that he proposed the rules with the idea of conforming as much as possible to the voltage groups yielded by the various apparatus used in current practice. In contradistinction to this, the principle accepted by the International Congress was that of adapting the lead thicknesses to the isodose curves as actually measured for different voltages, this necessitating four steps between 100 and 200 kv. In the light of the critical measurements of van der Tuuk and Boldingh the author now suggests two possible new modifications of the German protective values. These apply to the voltages between 150 and 200 kv., the first recommending 2.5 mm. lead from 125–160 kv., and 3.5 mm. lead from 160–200 kv.; the second recommending as in the International rules 2.5 mm. lead from 125 to 150 kv., 3 mm. from 150–175 kv., but only 3.5 mm. from 175–200 kv.

It is agreed by the author that the value of 5 mm. lead recommended both by the International Congress and by the German Roentgen Society for 200–220 kv. is too high, 4.5 mm. lead being entirely sufficient. A change to this effect might therefore be advisable.—*T. Leucutia.*

Joly, Marcel. Protection contre le rayonnement X au cours des séances de radiothérapie profonde. (Protection against roentgen rays during the administration of deep roentgen therapy.) *Bull. et mém. Soc. de radiol. méd. de France*, Oct., 1930, *18*, 354–355.

The author has constructed a protective cage which can be placed around the treatment table thus hermetically inclosing the patient irradiated. The use of such an arrangement cuts out all the radiation from the tube as well as the scattered radiation from the patient so that no protective control cabinets are necessary for the operator. It also permits the treating of several patients in one room.—*T. Leucutia.*

Bouchacourt, L. Sur la protection des radiologistes pendant les examens radioscopiques. (The protection of the radiologist during roentgenoscopic examination.) *J. de radiol. et d'électrol.*, Sept., 1930, *14*, 489–494.

In this article the author summarizes the present protective measures recommended for roentgenoscopy. The enclosure of the tube within a lead box, the providing of the roentgenoscopic screen with a lead glass, and the wearing by the roentgenologist of glasses, lead apron and bonnet will as a rule give sufficient protection against the effect of the direct rays. For the protection against the secondary rays, the author advises the use of the integral protector of Belot or some similar apparatus.

Protection against shock from the high tension current is necessary only in case of reduction of fractures or localizations under roentgenoscopic control. For this purpose the table of MacCutchen with biplane roentgenoscope (the tube transformer being oil-immersed) is recommended.—*T. Leucutia.*

Spiegler, Gottfried, and Juris, Kalman. Ein neues Kopierverfahren zur Herstellung ideal harmonischer Kopien nach kontrastreichen Negativen. (A new process for the making of ideal harmonic prints from negatives rich in contrast.) *Fortschr. a. d. Geb. d. Röntgenstrahlen*, Oct., 1930, *42*, 509–518.

After discussing in detail certain fundamental principles of photography such as gradation, detail and harmony, the authors describe a new procedure for the making of good prints from negatives too rich in contrast. The procedure is as follows: A diapositive is printed first by leaving a space of 1 cm. between the original negative and the diapositive film so as to produce a somewhat blurred image. This diapositive is then used as a filter during the printing of the positive, being placed between the light source and the original negative again at a distance of 1 cm. The positive print is thus exposed for a short time; then the diapositive filter is removed and the print further exposed through the negative alone.

Several positive roentgenograms printed both by the usual procedure (through the negative alone) and by the authors' procedure (with interposition of the diapositive filter) are reproduced to show the value of the method.—*T. Leucutia.*

Naujoks, H. Die Entwicklung der Kinder, die nach temporärer Strahlensterilität der Mutter geboren wurden. (Development of children born after temporary roentgen sterilization of the mother.) *Strahlentherapie*, Aug. 9, 1930, *37*, 572–583.

Reports are given of 6 children born of mothers who had been temporarily sterilized with roentgen rays. There was no definite proof of roentgen injury in any of the cases though there were anomalies in some of the children. The first child had a disturbance of speech which seven years ago was distinct stuttering but is now only a slight lisp which may be due to adenoids. It hardly seems probable that this anomaly was caused by roentgen injury. The second and third children were born after a long period of sterility and neither of them showed any evidence of roentgen injury. In the fourth case the mother was amenorrheic for two years and then menstruated for four years before she became pregnant. This child was normal up to his death at two years of age from bronchopneumonia. In the fifth case the child had retarded physical and psychic development but it may have been due to rickets and the very bad conditions under which it lived. There has been an improvement recently—the child is now $3\frac{1}{4}$ years old—but the mother says there

are still signs of inferiority. It is very hard in this case to say whether the injury was caused by the rays. The sixth child is obese and has neuropathic symptoms. But obesity is a family trait in this family. Her vision is normal and there were no pathological findings in the eyegrounds.

To definitely decide the question of roentgen injury of the children all such children should be carefully examined and followed up with the cooperation of pediatrists and students of heredity.—*Audrey G. Morgan.*

CASPARI, W. Über die Ernährung der Krebskranken. (The diet of cancer patients.) *Strahlentherapie*, Sept. 2, 1930, *37*, 719–734.

The author discusses the work that has been done on diet in cancer and concludes that the diet should be low but adapted to the patient's condition for of course a patient who is weak anyway should not be further weakened by too strict a diet. But even in these cases long-continued over-feeding is to be avoided. The diet should be poor in carbohydrates and particularly in fresh vegetables and sugar. Bread and cereals, particularly wheat and corn, can be used in moderate amounts, also potatoes. Protein and fat can be given in any desired amount not inconsistent with the first requirement of a low diet. The action of vitamin A in increasing resistance can be utilized without increasing the caloric value of the food too much by using cod-liver oil. Raw food is dangerous. Large amounts of eggs and milk should not be used. Moderate amounts of milk do no harm. Liver and tomatoes are forbidden. Salt may be given as desired until more is known on this point. Giving a mixture of salt rich in calcium and magnesium and poor in potassium as a medicament may be useful. This diet is particularly indicated for patients after operation or irradiation. In such cases fluid should at first be given abundantly and then decreased. Care should be taken to keep the intestines moving freely.—*Audrey G. Morgan.*

SURMONT, J. Sur un point de technique téléradiographique du coeur et des vaisseaux de la base. (On a technical point of teleroentgenography of the heart and great vessels.) *Bull. et mém. Soc. de radiol. méd. de France*, July and Nov., 1930, *18*, 321–330 and 371–373. See also *Presse méd.* Jan. 28, 1931, *39*, 131–133.

Teleroentgenography of the heart, made at a distance of more than 1 meter 50 cm., was severely criticized by Bordet, since it does not permit an exact localization of the G point (G indicating the junction of the middle or pulmonary and of the inferior or ventricular arc) or the point of the apex. The author uses opaque landmarks for the determination of the normal ray, on the one hand, and of point G and the apical point, on the other. The landmarks are mounted on a specially constructed cassette.

In discussing the technique of a good teleroentgenogram the author insists on the following factors: A good immobilization of the patient is essential. The position of the clavicles and thorax must be rigorously symmetrical on the two sides. The anticathode film distance must be exactly measured so as to be able to make the necessary corrections for the various diameters of the heart. The best results were obtained by taking instantaneous (0.1 sec.) roentgenograms during diastole. For this purpose the technician holds the radial pulse of the patient or he may use a sphygmomanometer. The exposure is made at the end of the systole. In making comparative studies of the diameters of the heart in systole and diastole, a variation as high as 1 cm. was found for the transverse diameter.

The conclusion is reached that by taking into consideration the above factors a very good teleroentgenogram of the heart may be obtained, this forming a complementary study to orthodiagraphy. The various diameters of the heart appear very precise.—*T. Leucutia.*

ACTION OF ROENTGEN RAYS AND RADIUM ON THE EYE AND EAR

EXPERIMENTAL DATA AND CLINICAL RADIOTHERAPY

BY

A. U. DESJARDINS

MAYO CLINIC

ROCHESTER, MINNESOTA

SECTION TWO

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ACTION OF ROENTGEN RAYS AND RADIUM ON THE EYE AND EAR

Analysis of Experimental Data

Roentgen Rays. The first step in analyzing the foregoing experiments is to divide them into three groups: (1) those in which the animals were irradiated before birth (in utero); (2) those in which rapidly developing eyes were exposed to roentgen rays soon after birth, and (3) those in which the fully developed eyes of adult animals were irradiated.

The studies of von Hippel (1905, 1906, and 1907), Bossuet (1909), and Pagenstecher (1916), show that irradiation of the pregnant uterus often leads to the death of the fetus and sometimes of the mother. So far as the eyes are concerned, these experiments indicate that prenatal irradiation may cause developmental anomalies of the lids and degenerative changes in the crystalline lens. The evidence, however, is not conclusive, either because of lack of adequate controls or because of insufficient or ambiguous data. Moreover, incomplete information about the technical factors makes it impossible to attribute the effects described to any particular factor. For example, it appears likely, as suggested by von Hippel (1906), that the palpebral anomalies noted may have been related to amniotic adhesions, but the connection between such adhesion and irradiation is not clear, especially since similar observations were not made in his subsequent investigations. The only other mention of such anomalies and adhesion of the amnion to the lids is to be found in the experiments of Little and Bagg (1923) on the occurrence of hereditary abnormalities among the descendants of irradiated mice. The anomalies of the eyelids observed by von Hippel (1906) and by Little and Bagg are of the same general character and probably have a common cause. Little and Bagg have apparently shown that such anomalies, acquired as the result of irradiation, are transmitted to the descendants through several generations. Should such a fact be confirmed by later investigation, it would tend to prove that such effects are caused, not by action of the rays on the tissues of the fetus, but on the germ plasm of the parents. The experiments of von Hippel (1906) and Little and Bagg differ in that the former did not find the peculiar abnormality of the eyeball described by the latter, but this discrepancy may well spring from the difference in the experimental conditions.

Besides developmental defects in the lids, von Hippel (1905, 1906, and 1907) also found changes in the lens of some of the fetuses. These changes ranged from slight opacity to actual cataract, but his studies were not sufficiently complete to enable him to be certain of the character of the changes or of their definite relation to irradiation. Indeed, the confusion of his report leaves no alternative but to share his uncertainty. These experiments suggest that prenatal exposure of the eye to radiation causes lenticular degeneration and cataract formation, but von Hippel was unable to exclude postmortem alteration as a partial factor, and the microscopic appearances were not unequivocal. Lenticular opacity, or cataract, was observed in only one of the young produced by the four females whose abdomen had been protected from direct irradiation. It is therefore permissible to assume that the ap-

parently frequent occurrence of cataract in the progeny of the first series of females exposed to direct abdominal irradiation was due, not to the direct action of the rays on the eyes of the fetus, but to action on the tissues of the mother. A possible indication of such indirect action is that, in one litter, extensive hemorrhage was found in the stomach and intestine. Such hemorrhage may have been the effect of irradiation on the relatively sensitive mucosa of the intestine or on the blood and blood-forming organs; indeed, the death of many of the irradiated mothers may have had a similar cause. Unfortunately, systematic necropsy on mothers and young was not performed. The occurrence of similar changes in the young after the injection of solutions of cholin into the mother makes it even more likely that the ocular abnormalities mentioned were the result of a general toxic effect produced by irradiation and by the injection of cholin.

The evidence submitted by Bossuet (1909), with reference to the ocular changes in the young resulting from abdominal irradiation of the mother, is not conclusive, but tends to confirm the observations of von Hippel, so far as the lens is concerned. Vacuolar degeneration and swelling of the lenticular fibers were the oustanding microscopic features described by both von Hippel and Bossuet, but if more satisfactory evidence were not available, a measure of doubt must persist. All doubt is dispelled, however, when we come to analyze the large number of experiments on the effect of roentgen rays on the rapidly growing eyes of young animals after birth.

The investigations of Chalupecky (1897), Tribondeau and Récamier (1905), Belley (1907), Tribondeau and Belley (1907), Tribondeau and Lafargue (1907), Bossuet (1909), and Frogé (1922), agree rather closely in showing that exposure to roentgen rays of the rapidly developing eyes of young animals may cause retardation of development of the eyeball and actual pathologic alterations in the lids, conjunctiva, cornea, lens, and iris. The effect of irradiation on the development of the eye is the greater, the younger the animal; this effect diminishes rapidly as age increases and varies in degree with the dose of roentgen rays and with the time elapsed between irradiation and observation. Retardation sufficient to cause marked difference in the size of the eyeball was commonly observed by Tribondeau and Récamier (1905), Belley (1907), Tribondeau and Belley (1907), Bossuet (1909), and Frogé (1922). Indeed, this was a constant effect of irradiating the eyes of very young animals when sufficient time was allowed subsequently for the difference to manifest itself. One might be tempted to ascribe such inhibition of growth solely to the influence of the rays on the eyeball itself, but the studies of Tribondeau and Récamier (1905), and of Bossuet (1909), show similar retardation of the bones and other structures included in the field of irradiation. According to Belley (1907), the growth of the irradiated structures does not cease completely, but proceeds at a reduced rate, and such retardation continues for a considerable time. There is no direct evidence to indicate how long such retardation may continue, but its duration probably depends on the age of the animal and on the intensity and duration of irradiation.

Conjunctiva and Eyelids. Tribondeau and Récamier (1905) and Belley (1907) noted that in animals irradiated soon after birth (before the normal opening of the eyelids) the lids opened sooner than in unirradiated animals of the same age. This might appear as evidence of a possible stimulating effect of the rays on the lids, but Belley's explanation is probably nearer the truth. According to Belley, the more rapid opening of the lids was due to increased destruction of the epithelial cells which

still kept the lids united. Regardless of the age of the animals, the ocular structures most sensitive to roentgen rays are the conjunctiva and lids. In all the experiments in which the eye was exposed to a sufficient dose of roentgen rays the first effects noted were loss of hair and cilia and inflammation of the conjunctiva and eyelids. The conjunctiva actually appears to be slightly more sensitive than the lids, because, as pointed out by Belley, the conjunctivitis generally antedated the blepharitis. This applies to the rapidly growing eyes of young animals irradiated soon after birth and also to the fully developed eyes of adult animals. The experiments of Scholtz (1902), Birch-Hirschfeld (1904), Tribondeau and Lafargue (1907 and 1908), Rollet and Malot (1914), Rauch (1904), Terrien and Clunet (1919), Rados and Schinz (1922), and Jacoby (1924) concur in showing that the action of roentgen rays on the fully developed eye of adult animals affects exclusively the anterior, superficial structures. The exceptions mentioned by Birch-Hirschfeld with reference to the retina and optic nerve will be considered separately. Again, as in the case of very young animals the conjunctiva and eyelids appear to be distinctly the most sensitive of the ocular structures. In most cases the dose of roentgen rays was considerably beyond the so-called erythema dose.[89] Rados and Schinz, for instance, exposed the eyes of their animals (rabbits) to doses from six to twenty-six times greater than the erythema dose for human beings, and from one and a half to five and two-thirds times the erythema dose for rabbits. The eyes exposed to one and a half, two and a third, and three times the limit of skin tolerance in rabbits were not at all affected.

Loss of hair and cilia from the lids is usually the initial manifestation, but does not appear until after a latent period of from one to two weeks, depending on the intensity of irradiation. The hair and cilia first become loose and can be readily extracted, but do not begin to fall spontaneously until a few days later. Accurate and detailed observations on the relative time of appearance of epilation, conjunctivitis, blepharitis, and keratitis were seldom made, and the evidence is not so definite as it might be. The observations of Rados and Schinz suggest that the conjunctivitis precedes the inflammation of the lids, but the reports of others on this point are not specific and give the impression that the conjunctivitis and blepharitis are essentially simultaneous. From a few days to one week after the onset of epilation, the palpebral and bulbar conjunctiva become red and injected and this is accompanied by increase in secretion. At the same time or soon afterward, the eyelids themselves become red, thickened and edematous. The increased conjunctival secretion may be mucous in character, or, if the irradiation has been sufficiently intense, the secretion may become mucopurulent or purulent, and these disturbances may continue for several weeks. When the dose has not been too great the alopecia of the eyelids is only temporary, and the lashes and hair grow again later. Belley and Bossuet were the only ones to observe that the regrowing hair is white at first, but that later the pigment also returns. Irradiation beyond a certain limit causes permanent alopecia and atrophy or actual ulceration of the lids. During the acute stage the inflammatory reaction of the conjunctiva and lids may be accompanied by photophobia, keratitis, and contraction of the iris. The early, slight, and transient conjunctivitis noted by Terrien and Clunet one day after irradiating the eye of ten rabbits was probably not due to roentgen rays, because the latent

[89] The erythema dose for the rabbit is between two and four and a half times the erythema dose for human skin.

period was much too short, but may well have been caused by the heat of the roentgen tube and exposure of the eyeball affecting the moisture of the conjunctiva. Irradiation sufficient to cause marked conjunctivitis also induces degeneration of the endothelial lining of the blood vessels; this is accompanied by perivascular leucocytic infiltration and is followed by regenerative hyperplasia of the endothelial cells, thickening of the vascular coats and narrowing of the lumen. Birch-Hirschfeld (1904) observed such changes in the conjunctiva and eyelids.

Lack of essential technical details in some of the experiments prevents an accurate analysis of the results of irradiation. However, the majority of the reports furnish sufficient information to establish the absolute relationship between the dose of radiation and the ensuing pathologic changes. For example, the studies of Rados and Schinz show that the eyes of adult rabbits exposed to doses varying between 650 and 1300 per cent of the human erythema dose remained unaffected, but that in the eyes exposed to doses varying between 1700 and 2600 per cent of the human erythema dose disturbances of the conjunctiva, lids, and cornea always developed, and that the degree of such alterations was a rough measure of the dose. Jacoby (1924) contended, apparently with justice, that the epilation dose for the eyelids of the rabbit, as given by Rados and Schinz, was too high. But, even if the validity of this contention should be granted, the main facts, nevertheless, are fully confirmed by others, including Jacoby. It seems clearly established, therefore, that the radiosensitiveness of the conjunctiva and eyelids is slightly greater than that of the surrounding skin of the face.

Cornea. The cornea appears definitely more resistant than the conjunctiva and lids, but may also be injured by excessive irradiation. Evidence of such injury, varying from mere dullness to actual ulceration, is to be found in the experiments of Chalupecky (1897), Scholtz (1902), Tribondeau and Récamier (1905), Belley (1907), Frogé (1922), Rados and Schinz (1922), and Jacoby (1924) on young and on adult animals. Points which tend to confirm the relatively greater resistance of the cornea to irradiation are that the keratitis appears later, is generally less marked, and subsides sooner than the conjunctivitis. In fact, the effect of the rays on the cornea usually consisted in mere dullness, and this disappeared in a few days. Only in the animals exposed by Chalupecky (1897), Frogé (1922), Rados and Schinz (1922), and Jacoby (1924) to strong single doses or irradiated daily or every second day for a long time, do we find evidence of actual destruction of the cornea. That ulceration of the cornea should have resulted from such extreme total intensity of irradiation is hardly surprising; the wonder is that even greater changes did not occur. All these experiments indicate that the sensitiveness of the cornea to roentgen rays is distinctly less than that of the conjunctiva and eyelids.

The microscopic features of such keratitis, as described by Chalupecky and by Jacoby, include irregular degeneration, destruction, and consequent thinning of the corneal epithelium, which, except around the limbus, is reduced to one or two layers of cells with indistinct outlines, vacuolization of the protoplasm, and deformation or disintegration of the nuclei. Leucocytic infiltration, sometimes extending into the substantia propria, especially around the vessels in the vicinity of the limbus, and swelling of the endothelial lining of the vessels, also are features of the reaction of the cornea to strong irradiation.

Iris. The iris appears to be even less susceptible than the cornea, and the only

change in this structure, so far as the rapidly growing eyes of young animals are concerned, was described by Belley (1907) as retardation in pigment formation; which is to say, that the normal changes in the color of the iris took place more slowly in the irradiated than in the unirradiated eye. Birch-Hirschfeld (1904) observed hyperemia and decoloration of the iris and ciliary processes, with swelling of the epithelium of the ciliary body. Iritis, with fibrinous exudate, loosening of the posterior pigment epithelium, and adhesions to the capsule of the lens were found occasionally by Bossuet (1909) in eyes which had been exposed to exceptionally strong doses and in which the inflammatory reaction in the conjunctiva and cornea had been especially severe. Frogé (1922) also noted slight iritis, with leucocytic infiltration of the ciliary body, but he regarded this as secondary to the more severe inflammation of the conjunctiva and cornea rather than as a direct effect of the rays on the iris. This deduction is supported by the experiments of Rados and Schinz and of Jacoby, who never found the slightest abnormality in the iris of adult animals, in spite of exposing the eye repeatedly to doses varying between 200 and 2600 per cent of the human erythema dose. It is probable, therefore, that inflammation of the iris after irradiation does not represent a specific reaction to the rays, but is secondary to the inflammation of the conjunctiva and cornea induced by the rays. Birch-Hirschfeld (1904) and Jacoby (1924) mentioned degeneration of the endothelium and swelling of the intima and muscularis of the blood vessels of the iris. These descriptions are not sufficiently explicit to give a clear idea of the effects of irradiation on the blood vessels, but they furnish additional evidence that the endothelium and media of the blood vessels are moderately susceptible to roentgen and radium rays.

Crystalline Lens. If the radiosensitiveness of the conjunctiva, eyelids, cornea, and iris is only slightly greater in young than in adult animals, the susceptibility of the crystalline lens, on the contrary, is much greater. The experiments of Tribondeau and Récamier (1905), Belley (1907), Tribondeau and Belley (1907), Bossuet (1909), and Frogé (1922) furnish conclusive evidence on this point. All these experiments show that irradiation of the eye in young, rapidly growing animals causes in the lens marked degenerative changes leading to cataract. These alterations consist in granular and vacuolar degeneration beginning around the periphery and extending inward toward the center of the lens. The first clinical indications of such lenticular alteration were noted by Belley on or after the thirty-third day following irradiation, but microscopic evidence was obtained much earlier in the form of a zone of vesicles around the margin of the lens. Tribondeau and Belley stated that the epithelium on the anterior surface of the lens is affected first and shows more or less extensive defects (destroyed cells), especially in the retro-iridian zone. Later the crystalline fibers themselves become swollen and tortuous. The description of the process given in the different experiments is essentially the same. Discrete vacuoles appear and gradually coalesce to form granular plaques, which spread throughout the lens until the entire structure becomes opaque. This is accompanied by irregular desquamation of the anterior epithelium, and these patches of desquamation are separated by areas of cellular proliferation which sometimes form definite nodules. The capsule of the lens slowly but gradually thickens until its anterior portion becomes twice as thick as the normal capsule, and more or less marked atrophy of the lens supervenes. Several months after irradiation the lens is sometimes only

half its normal size. Moreover, the depth of the anterior chamber increases as the atrophy of the lens progresses.

If the lens of young animals is so sensitive to irradiation, the lens of adult animals, on the contrary, is remarkably insensitive, even to doses of roentgen rays several times stronger than the doses used in treating human beings. This is conclusively shown by the experiments of Scholtz (1902), Tribondeau and Lafargue (1907 and 1908), Rauch (1914), Rollet and Malot (1914), Rados and Schinz (1922), and Jacoby (1924), in none of which was any abnormality of the lens noted after irradiation, although the eyes of many adult animals were exposed to doses sufficient to cause marked ulcerative radiodermatitis of the lids and keratitis sometimes bordering on perforation. Tribondeau and Lafargue (1908) presented to the members of the Société de Biologie a young cat, each eye of which had been exposed to strong roentgen irradiation one and two months, respectively, after the opening of the lids. In the eye first subjected to the rays, one month after the opening of the lids, cataract developed, but the other eye, irradiated two months after the opening of the lids, remained normal, in spite of having received a dose twice as strong as that given to the eye exposed one month earlier. The conclusion seems warranted that the mature crystalline lens of adult animals possesses a high degree of resistance to irradiation. Nevertheless, even the mature lens of adult animals can be made to undergo degeneration by sufficiently strong irradiation, as was shown by Bossuet in two rabbits and two guinea pigs.

Aqueous and Vitreous Humors. The only changes in the aqueous humor observed by Belley (1907), Bossuet (1909), and Frogé (1922) consisted in flakes of exudate and leucocytic infiltration, probably secondary to the inflammation of other structures.

Retina. The experiments of Tribondeau and Récamier (1905), Belley (1907), Tribondeau and Belley (1907), and Frogé (1922), in which the eyes of young animals were exposed to roentgen rays soon after birth, agree in showing that the outstanding effect of irradiation on the retina consists in retardation of development affecting only the internal granular layer. The other layers appear to develop normally, and this circumstance, together with the retardation of development of the eyeball as a whole, causes the external granular layer and the layer of rods and cones to assume a peculiar plicated appearance characterized by multiple folds of the anterior half to two-thirds of the retina. In some instances this peculiar formation was so marked as to resemble the acinous formation of the gastric glands. Groups of external granular cells at the bottom of some of the folds were sometimes isolated as buds and closely resembled the "rosettes" once described by Wintersteiner as pathognomonic of glioma of the retina. The essential relationship of these rosette formations to retinal glioma has never been accepted and has long since been forgotten. The general view has been well expressed by Leber, who regards the rosettes as due to the sectioning of folds of the retina caused by incomplete development of the eyeball. Pagenstecher (1916) found similar rosettes in the retina of fetuses which had been irradiated in utero, and wisely attributed them to the microphthalmia induced by the rays. Further evidence of such association was furnished by Fräulein Lindenfeld, who described similar rosettes observed in the microphthalmic eyes of one fetus five to six months old and one seven to eight months old, the abdomen of whose tuberculous mother had been irradiated with the object

of sterilization. Moreover, Belley stated that the degree of such plication corresponded roughly with the duration and intensity of irradiation and with the subsequent period of observation. The only animals in which this effect was not observed were those in which the dose of radiation had been small or which had been killed too soon after exposure. Hence, there can be little doubt that this change in the retina of very young animals following irradiation must be a direct effect of the rays; no such alteration was noted in the unexposed eye of the same animal or of other, control, animals of the same age.

Aside from retardation of development of the internal granular layer and of the eyeball as a whole and the resulting plication of the anterior portion of the other retinal layers, no other alteration of the retinal coats was found. Frogé did find changes in the layer of rods and cones in one of his animals, but, since nothing similar occurred in the remaining animals, he was probably right in attributing such change to the marked inflammatory reaction which this eye had undergone. Bossuet also observed "pronounced changes in the retina," but his failure to describe them leaves us in the dark. The optic nerve also remained unaffected, regardless of the dose of roentgen rays to which the eye was exposed. This is in accord with the high degree of resistance to radiation which nerve tissue generally is known to possess.

Exposure of the fully developed eye of adult animals, even to doses of roentgen rays sufficient to cause marked conjunctivitis, dermatitis of the lids, and keratitis, does not appear to exert an appreciable influence on the retina. At least, this is the only conclusion which can be drawn from the experiments of Tribondeau and Lafargue (1908), Rollet and Malot (1914), and Rados and Schinz (1922). On the contrary, Birch-Hirschfeld (1904) and Jacoby (1924) described what they took to be pathologic changes in the retina due to irradiation. These alterations consisted in degeneration of some of the ganglion cells, with shrivelling, intense staining, and granular disintegration or actual disappearance of the nuclear chromatin, and vacuolization of the protoplasm; loosening of the nerve fiber and inner plexiform layers; reduction in size of the inner granules, which, like the outer granules, were rounded and stained homogeneously; granular disintegration of the outer segment of rods and cones, and uniform myelin degeneration of the optic nerve, some of the fibers of which had disintegrated. In some of his animals, Birch-Hirschfeld noted that the papilla was gray, the medullary wings slightly faded, and the retinal vessels indistinct. Jacoby also noted vacuolar degeneration of some of the ganglion cells of the retina in two animals and beginning degeneration of the inner granular layer in one of the only two animals whose irradiated eye was examined microscopically.

Such marked divergence in the results of these two groups of experiments is not easy to understand. Mere difference in dosage can hardly account for the discrepancy, because the doses of roentgen rays employed in some of the experiments of the first group were even greater than those used in the second. Some of the animals irradiated by Tribondeau and Récamier (1905), Belley (1907), Tribondeau and Belley (1907) and Tribondeau and Lafargue (1908) received doses of roentgen rays from two to four times as strong as those used by Birch-Hirschfeld. The degree of the retinal abnormalities described by Birch-Hirschfeld does not bear any clear relation to the dose of roentgen rays to which the eye of the different animals was subjected. Moreover, the reports of Birch-Hirschfeld are not specific about the provision of adequate controls. Under these circumstances, it is possible that the

pathologic changes ascribed to irradiation, that is to say to a direct effect of the rays on the retina, may have been rather a result of the intense inflammatory reaction of the conjunctiva, eyelids, cornea, and perhaps also of the systemic reaction to irradiation. The explanation advanced by Birch-Hirschfeld, that the variability in the degree of the changes noted in the anterior and posterior segments of the eye was due to a difference in the penetrating power of the rays, is based on an obvious misconception.

Tribondeau and Lafargue (1908) contended that, when the irradiated eyes were plunged in fixative immediately after enucleation, they were never able to find changes such as those described by Birch-Hirschfeld, in spite of the fact that some of these eyes had received doses of radiation much greater than the doses used by Birch-Hirschfeld. Such changes were often noted, however, in the retina of unirradiated eyes when the eyeball had been opened and left in the open air, even for a few minutes, or had been fixed in liquids with a formalin or sublimate base. Morphologic variations of the ganglion cells closely simulating pathologic changes had also been observed in unirradiated and apparently normal eyes. Tribondeau and Lafargue attributed the loosening of the inner plexiform layers noted by Birch-Hirschfeld to improper fixation; they ascribed the homogeneous aspect of the external granules to their great colorability, and the granular appearance of the outer portion of Jacob's membrane to oblique section of the rods. Moreover, they justly pointed out that, if the uniform degeneration of the optic nerve found by Birch-Hirschfeld in two of his five animals is accepted as an effect of irradiation, loss of vision should ultimately have ensued. To test this they irradiated both eyes of one rabbit for one hour and kept the animal for five months, but careful histologic examination failed to yield the slightest evidence of retinal degeneration or optic atrophy. On the whole, the retina and optic nerve of animals more than two or three months old appear to possess remarkable resistance to roentgen rays, and the evidence to the contrary is not strong. It is probable that the changes described by Birch-Hirschfeld and by Jacoby were due to defects in technique or were secondary to inflammation induced by irradiation in other more sensitive structures. The same is undoubtedly true of the marked dilatation of the retinal veins observed by Rauch in three animals whose eyes had been exposed to strong doses.

The experiments of Little and Bagg (1923) indicate that the progeny of adult rabbits, whose generative organs have been exposed to roentgen rays, exhibit various abnormalities including microphthalmia, with necrosis of the eyelids and subsequent blindness, acephaly, shortening and upward deviation of the upper jaw, shortening of the foreface, irregular arrangement of the teeth and abnormal development of the extremities; these lesions appear to be transmitted to the descendants in a mendelian ratio. The fact that the lesions were transmitted to the descendants of the irradiated mice through more than one generation speaks against a direct effect of the rays on the fetus and in favor of an influence on the genetic cells of the parents. The lack of proper controls, however, diminishes the value of these experiments, which remain unconfirmed. Since these studies deal with the effect of roentgen rays on the reproductive organs, no further allusion to them will be made here, except to point out that abnormalities such as those described by Little and Bagg can be induced in the offspring only when the sexual glands of the parents are exposed to the direct action of the rays; such effects cannot result from irradia-

tion of other regions of the body than that in which the genital glands are situated.

Effect of Roentgen Rays on Tuberculosis of the Eye. The experiments of Jendralski (1922) and Stock (1926) indicate that roentgen rays have a definite influence on tuberculous lesions of the eye. The effect of the rays seems to be greatest during the the infiltrative stage of the tubercle and least after its caseous degeneration. This observation gives color to the idea that the action of the rays is chiefly to destroy the infiltrating leucocytes, especially since the rays have no bactericidal effect on the bacillus of tuberculosis. This interpretation is supported by the observations of Stock, who noted disintegration of the infiltrating lymphocytes as the initial phase of the changes in and around the tubercles induced by irradiation.

The investigation by Sabbadini (1924) of the effect of roentgen rays on infected traumatic ulcers of the cornea shows an apparent resolving influence on the inflammatory process, but the mechanism involved has not been elucidated. The validity of Sabbadini's attribution of this effect to secondary rays generated by metals of high atomic weight placed in contact with the ulcerated cornea during irradiation is uncertain.

Radium. If we may judge by the foregoing reports, many of the experiments on the action of radium on the eye hardly deserve the name, because these reports fail to specify the number, age, or sex of the animals, the precise form and manner in which radium was employed, the kind and degree of filtration, the distance between the radium and the tissue exposed, the duration of each individual exposure, the total duration of the separate exposures, and the exact interval between each exposure, or other technical data essential to a detailed analysis of the effect of radium on the ocular structures. It is, therefore, impossible to draw any but general conclusions.

The experiments of Birch-Hirschfeld (1904), Milroy (1905), London (1906), Roselli (1907), and Chalupecky (1911) concur in showing that the effect of radium on the eye is essentially the same as that of roentgen rays, and that exposure to sufficient doses of radioactive substance causes an inflammatory reaction in the conjunctiva, eyelids, cornea, iris and ciliary body, and retina. It is not surprising that doses such as those used by Roselli should have had no effect, especially if the short time allowed for such effects to take place is taken into consideration. Under such conditions, it is doubtful if any perceptible effect could have been noted at any time. The slightly larger quantity of radium used by Chalupecky (1911) for a longer time caused severe inflammation of the ocular and palpebral conjunctiva, as well as of the cornea. The conjunctiva and cornea became greatly swollen and covered with exudate, and the pupil contracted, but the iris, lens, and retina appeared not to have been affected. It is not clear whether Chalupecky's failure to mention radiodermatitis of the eyelids means that such inflammation did not occur or whether its absence indicates that the lids were not exposed directly to radium.

London (1906) exposed the entire body of three rabbits to 0.26 cg. of radium for an unknown period; the distance between the radium and the animals, as well as the character and degree of filtration, were not mentioned. The statement was made, however, that the animals did not exhibit ill effects for fifteen days, a latent period corresponding closely to that incident to roentgen irradiation. Subsequently, disturbances of the skin, nervous system, eyes, sexual function and general metabolism supervened, but London's failure to describe such changes prevents a satis-

factory analysis. For example, it is impossible to ascertain to what extent the ocular alterations may have been due to the direct action of radium on the structures of the eye and to what extent such changes may have been secondary to the influence of radium on other organs or on the body as a whole. The mere mention of central retinitis or neuritis only serves to add to the confusion. Certainly there is little ground for London's assumption that the retinal vessels and optic nerve are especially sensitive to the rays, particularly if the relatively great resistance of these structures to roentgen rays is borne in mind. The only useful bit of evidence lies in the mention of "pronounced ectropion from radiodermatitis of the lids" in one animal.

A consideration of the experiments of Birch-Hirschfeld emphasizes the similarity between the effects of radium and roentgen irradiation. Indeed, with one or two exceptions, these effects are practically identical. As in the case of roentgen rays, exposure of the eye to radium is followed, in adult animals, by a latent period of from one to three weeks. After this period, during which no abnormality is perceptible clinically, loss of hair and cilia from the lids, conjunctivitis, palpebral dermatitis sometimes to the point of ulceration, keratitis, and fading of the color of the iris develop. Within certain limits, the degree and duration of such disturbances are proportional to the intensity of irradiation. The inflammatory reaction then gradually subsides and may disappear without leaving any trace or may leave permanent evidence of its passage in the form of alopecia and sometimes scarring of the lids. The pathologic changes representing the foregoing clinical manifestations are of the same general character as those caused by roentgen rays. Again acute degenerative or destructive changes are found in the epithelial cells of the conjunctiva, eyelids, and cornea, especially in the basal layer (leucocytic infiltration); swelling and proliferation of the endothelium lining the blood vessels; degeneration of the vascular endothelium and partial disintegration of the pigment cells of the iris; hyperemia of the ciliary body; more or less marked degeneration of the ganglion cells and of the inner and outer granular layers of the retina, and myelin degeneration of the optic nerve. These changes, however, were even less constant with radium than with roentgen rays, and it is even more difficult to relate the degree of such changes to the dose of radium. Evidence of conjunctivitis, keratitis, and iritis sometimes continued for several months. Although there can be no doubt that the inflammatory reaction in the conjunctiva, eyelids, cornea, and probably also in the iris, represents a direct effect of radium, it is possible that the changes in the iris may be partly secondary to the inflammation of the other structures mentioned. Birch-Hirschfeld pointed out that changes in the blood vessels were perceptible only after a long interval. The integrity of the crystalline lens was never affected. With reference to the retinal alterations, it is interesting to note Birch-Hirschfeld's statement that these changes are not specific, because similar changes occur after experimental amaurosis with quinine, felix, methyl alcohol, division of the optic nerve, and as postmortem changes. This gives additional color to the contention of Tribondeau and Lafargue with reference to the supposed roentgen-ray changes in the retina described by Birch-Hirschfeld. His attempt to demonstrate the initial effect of radium on the retina by irradiating pieces of retina from the enucleated eye of a rabbit and his interpretation of the ensuing changes as due to radium are surprising, to say the least.

The experiments of Milroy (1905), in which 20 mg. of radium were used under conditions which allowed practically all the beta and gamma rays to exert their action on the embryos of chicks, apparently show that the integrity of the retina suffered more than that of the other ocular structures. No mention is made of inflammatory changes in the lids, conjunctiva, cornea or lens. Although the evidence is not clear, the impression is gathered that the development of the eyes continued for a time after irradiation, and that the abnormalities in the retina did not become perceptible until from two to three weeks after exposure. These retinal alterations consisted in general degeneration of all the cells, with disintegration of the ganglion cells and of the fibers of the optic nerve. In spite of the foregoing, Milroy stated that radium did not cause any reaction in the cells which respond normally to light. The radium in these experiments was in close proximity to the shell of the egg; therefore, not only the eyes, but the entire embryo was irradiated. Under such conditions, it is probable that the retinal changes described must have been a result of the influence of radium rays on the embryo as a whole, and cannot be accepted as representing the direct effect of radium on the eye. Otherwise, the results obtained by Milroy would have to stand in opposition to all other evidence on the subject. It is difficult to understand how abnormalities of the retina such as those described by Milroy could be caused directly by radium without any developmental or organic effect on the other ocular structures, such as the conjunctiva, eyelids, cornea, and crystalline lens.

The experiments of Meisner (1924), on the contrary, furnish reasonable evidence that radium introduced into the vitreous leads to lenticular opacity and some retinal degeneration, and that such are direct effects of irradiation. This evidence, however, is not sufficient to indicate the ocular structures which are most affected or which are the earliest to react to the rays.

Radioactive Water and Thorium X. The injection of a small quantity of radioactive water under the conjunctiva was shown by Chalupecky (1911) to have practically no effect on the eye, probably because the fluid is absorbed so rapidly that the radioactive substance does not have time to act. The only effects of injecting radioactive water directly into the vitreous are temporary haziness of the vitreous and cornea, and increase in intraocular tension. The haziness of the vitreous and cornea disappears in a few days.

Abelsdorff (1914) apparently demonstrated that even a small quantity of thorium X in solution, when injected into the anterior chamber of the eye, causes inflammation of the iris and sometimes of the cornea and conjunctiva. The iritis develops within from twenty-four to seventy-two hours and is characterized clinically by diminution in the size of the pupil, posterior synechiae, petechial hemorrhages, and a gradual loss of pigment. The pathologic features of such iritis are: clumping of the pigment granules, degeneration of the chromatophores, increase in the Klumpenzellen, and marked hyperemia and petechial hemorrhages of the iris and ciliary body. This inflammatory reaction disappears after several weeks, but, except after small doses of thorium X, the iris undergoes progressive atrophy. The endothelium of the iridian vessels is partly destroyed, and the media also is affected. Injection of a solution of thorium X into the vitreous causes, within from a few hours to a few days, cloudiness of the vitreous, narrowing and occasional occlusion of the retinal vessels, and multiple hemorrhages. Later, atrophy of the medullary wings in the

anterior section of the optic nerve and, after from one month to one and a half months, foci of chorioretinitis in the form of white flecks studded with black pigment are perceptible in the fundus. Areas of slight opacity in the posterior cortical surface of the lens are occasionally noted, but the lens remains generally clear. Decoloration of the iris, flecks of albumin in the vitreous and aqueous humors, hyperemia of the choroid and ciliary body, partial sloughing and hydropic swelling of the pigment epithelium, disappearance of the layer of rods and cones from the retina, marked degeneration of the internal granular layer and the layer of nerve fibers, and numerous hemorrhages in the retina, with partial destruction of the endothelium and thrombosis of the retinal vessels, also may occur.

The changes found by Stargardt (1915) in a series of similar experiments were substantially the same, but even more pronounced. Although evidence of inflammatory reaction in the anterior segment of the eye was not obtained, marked degenerative changes in the retina and choroid, and especially in the blood vessels, were noted. The vascular degeneration and tendency to hemorrhage described by Stargardt might be thought to indicate a greater tendency of radium to act on the blood vessels, but such apparently greater effect was due to the intimate relation of the radioactive substance (thorium X) to the vessels provided by the intraocular injection. The degree of optic atrophy varied with the period of survival and the dose of thorium X injected. Unlike Abelsdorff, Stargardt found constant degeneration in the crystalline lens several months after the injection, and was probably right in regarding this as a direct effect of irradiation. Abelsdorff did not observe such lenticular degeneration, probably because his animals were killed too soon after injection of thorium X or because the dose of thorium injected was smaller.

Effect of Radium on Tuberculous Lesions. Flemming and Krusius (1911) and Takahashi (1925) endeavored to ascertain the influence of radium as such, or as mesothorium, on tuberculous processes in the eye. The experiments of Flemming and Krusius indicate that both radium and mesothorium retard the development of the tubercles and that mesothorium also prolongs the incubation period. The absence of technical details in their report prevents any critical review of their data. However, the more complete and systematic investigation carried out by Takahashi furnishes substantial evidence that radium, in suitable doses and under proper technical conditions, has a striking inhibitory effect on tuberculosis of the conjunctiva, cornea, and iris. This is the more remarkable because Takahashi's further studies failed to show any direct effect of radium on the bacilli themselves. The interesting explanation advanced by Takahashi that the action of radium on the tubercles is due to an increase in the protein content of the aqueous humor deserves consideration; but what induces such increase in the protein content of the aqueous humor? It is probable that irradiation causes the disintegration of some of the leucocytes, notably the lymphocytes, infiltrating the tubercles and forming an important element in the defensive barrier against the *Mycobacterium tuberculosis*. The disintegration of such cells may liberate the protective substances within them and make them more diffusible in and around the tubercle and thus increase their effectiveness. The experiments of Stock (1926) tend to substantiate this view which, if confirmed by subsequent investigation, would provide a satisfactory explanation of the influence of radiation on tuberculous processes.

Clinical Considerations

Diseases of the Eyelids. Many of the experiments on animals have shown that the radiosensitiveness of the eyelids is slightly greater than the surrounding skin of the face; excessive irradiation causes the lashes and hair to fall from the lids, either temporarily or permanently, and the lids themselves undergo a more or less marked inflammatory reaction. Such inflammation subsides spontaneously and may disappear without leaving any traces or it may be followed by atrophy, telangiectasis and sclerosis. In other words, the skin of the lids behaves like the skin in other regions of the body.

Certain inflammatory diseases of the lids, on the other hand, appear to be favorably influenced by suitable doses of roentgen rays. BUNTING (1907) related the instance of a man aged twenty-five with progressive bilateral blepharitis complicated by frequent attacks of conjunctivitis and keratitis, who had been treated by various methods for two years without success and whose lids had become ulcerated, swollen, and devoid of lashes. His eyes were then exposed to roentgen rays for from eight to ten minutes every five days; all pain ceased after the second irradiation, and complete cure was obtained. MARQUES (1908) reported the cure of a man aged eighty, with lupus vulgaris of the lids, and three patients with chronic blepharitis associated with tuberculous conjunctivitis were reported by HENSEN and SCHÄFER (1924) to have been cured by roentgen irradiation. Other examples of cure or improvement following exposure to radiation have been furnished by KUMER and SALLMANN (1924), LANE (1924), BROEMAN (1925), PORDES (1926–1927), and others. In one case described by Pordes only one eye was exposed to the rays, and improvement and cure of the condition occurred only in the irradiated eye; the disease in the other eye continued unabated. KUMER (1923), Broeman (1925), and others have demonstrated that xanthelasma can be cured by radium. KEMPSTER (1915) also called attention to the value of irradiation in trichiasis and reported the cure of a patient by roentgen-ray treatment. An example of blastomycosis of the eyelid cured by radium was given by NEW and BENEDICT (1920).

Follicular Conjunctivitis. A few instances have been recorded which indicate that this variety of conjunctival inflammation sometimes reacts favorably to roentgen and radium rays. Thus PARDO (1904–1905) announced the cure of one patient treated with roentgen rays, and JACOBY (1906) of two patients treated with radium, COHN (1905) claimed to have cured seven patients supposedly suffering from trachoma or follicular conjunctivitis. UHTHOFF (1905) contended that the diagnosis of trachoma could not be sustained and that Cohn's patients undoubtedly represented examples of follicular conjunctivitis. COUTARD and OFFRET (1920) gave an excellent description of a lithographer's young apprentice who had suffered from marked follicular conjunctivitis since the age of four. Microscopic examination of the conjunctiva was made before and after treatment. Only the left eye was subjected to roentgen irradiation[90] seven times at weekly intervals. Four days after the second irradiation the follicular lesions had disappeared from the upper lid (the lower lid had not yet been treated), and all evidence of inflammation disappeared from both lids in the treated eye after the fifth exposure. The microscopic appearance of a section of the conjunctiva exposed to the rays exhibited a striking difference charac-

[90] Total dose, 12 Holzknecht units

terized chiefly by almost complete disappearance of the lymphocytic infiltration and thickening of the epithelial layer.

Van Duyse (1905) recorded the case of a young man aged twenty-three, with syphilis and nodular, proliferative, lymphomatous infiltration of the bulbar conjunctiva; the condition had increased progressively for several weeks, but diminished rapidly and disappeared completely after six roentgen irradiations at intervals of two or three days.

Parinaud's Conjunctivitis. Benson and Clay (1921) reported a case of this disease in which they had given treatment with radium. The patient was a woman aged seventy-two. Follicular conjunctivitis, which had developed after surf bathing in 1915, subsided promptly under local treatment. In 1917 and 1918 similar attacks occurred which again responded to treatment, but in 1919 symptoms in the right eye recurred, and local treatment proved unavailing. The condition was characterized by marked hypertrophy of the conjunctiva and pannus of the cornea, and sections of the hypertrophied conjunctiva showed "purely lymphoid tissue." Two applications of 50 mg. of radium for one hour on alternate days caused the inflammatory manifestations to diminish and to disappear almost completely in a month. The improvement continued steadily and tendency to recurrence was not observed.

Trachoma (Granular Conjunctivitis). The earliest account of trachoma treated with roentgen rays was given by Mayou (1902), who reported the case of a girl aged fourteen with bilateral trachoma and a thick, fleshy pannus in both eyes; the left eye was completely cured after twenty-two three-minute exposures to soft roentgen rays; the right eye, treated with a solution of copper sulphate, improved much less in the same time, but eight exposures to roentgen rays completed the cure of this eye also. A slight recurrence three months later cleared up entirely after four additional irradiations and the child remained well. In 1903 Mayou reported having treated fifteen other patients with roentgen rays and described nine, all of whom were influenced favorably and five were permanently cured; the others had recurrences or were still under treatment. The irradiations, which were directed to the everted lids with the rest of the face shielded by a metal mask, were carried to the point of causing slight conjunctivitis and epilation of the lids, but this soon subsided and the eyelashes grew again; the eyes remained normal in every other respect. Mayou attributed this remarkable effect on the lesions of trachoma to leucocytosis supposedly induced by the rays. Stephenson and Walsh (1903) recorded two cases of trachoma cured by roentgen rays. In each case only one eye was exposed to the rays, the other eye being left unirradiated to serve as a control. The disease disappeared from the irradiated eye after seventeen and six exposures, respectively, but the condition did not abate in the unexposed eye.

Bettremieux (1903) mentioned three cases in which he thought improvement had occurred more rapidly under roentgen irradiation than by ordinary methods of treatment. Cassidy and Rayne (1903) reported that a patient who had suffered from trachoma for nine years had been completely cured by prolonged roentgen-ray treatment through the lids. Geyser (1904), Goldzieher (1904), Pardo (1904), Vasyutinski (1905), Horniker and Romanin (1905), Pardo (1904–1905), Stargardt (1905), Thielemann (1905), Newcomet and Krall (1906), Kassabian (1906), Coleman (1907), Stargardt (1912), Jacqueau, Lemoine, and Arcelin (1920), Rollet and Bussy (1920), Cochard (1921), Meldolesi and Sabbadini

(1923), Meldolesi (1924), Lane (1924), Sabbadini (1926), and others, have submitted evidence that roentgen rays exert a definite, and often marked, influence on the manifestations of trachoma. It is true that in some of the patients reported as cured the trachomatous manifestations recurred, but it is equally true that many others remained free from the disease, either permanently or for a long time. Cochard (1921) was able to cure two patients permanently and to bring about the marked improvement of six others, but some of these had recurrence later. Resumption of treatment, however, was again followed by rapid decrease and disappearance of the granules, and this led Cochard to the probably sound conclusion that the initial treatment had not been sufficiently thorough or had not been continued long enough. Only two of the eleven cases included in his thesis failed to show any beneficial effect, and in these cases the disease had been of long standing and was associated with sclerosis and deformities of the lids.

Harman (1905) apparently was the only one to report complete failure to influence trachoma by roentgen rays. It is permissible to surmise, therefore, that his technique may have been faulty. Terrien (1919) stated that irradiation causes regression of the lymphoid hyperplasia and disappearance of the granulations, but that recurrence is the rule. Derby (1924) also wrote disparagingly of the value of roentgen-ray treatment in trachoma; his opinion was based not on personal experience, but on a cursory and obviously incomplete review of the literature. It is impossible to read the communications of Thielemann (1905), Cochard (1921), and Sabbadini (1926), to mention only these three, without being convinced that roentgen rays have a real and substantial effect on the lesions of trachoma. This effect appears to be greatest in the early stages of the granular form of the disease, but it is also observed in the other varieties. Irradiation has little if any effect, however, when the inflammation has been present so long as to have caused sclerosis and distortion of the lids.

The early attempts to treat trachoma with roentgen rays were made by irradiating the conjunctiva of the everted lids directly. This is not surprising if the slight power of penetration of the long wave-length rays then available is borne in mind. But, as early as 1903, Cassidy and Rayne showed that eversion of the lids for direct exposure of the conjunctiva is unnecessary, and that equal results can be obtained by irradiation through the intact lids. Moreover, the large number of exposures required during the early days, because of unperfected roentgen tubes and generating apparatus, would now be uncalled for. Meldolesi and Sabbadini irradiated the eyes of their patients by the Ghilarducci method[91] of secondary radiators, and credited it with superior results. Comparison of their cases with those of others, however, does not give much strength to their claim. The superiority of their results is hardly great enough to be convincing, and any such superiority as may exist may well be due to more thorough irradiation. So far as permanency of cure is concerned, it is possible, if not indeed probable, that technical factors may have a significant influence, but it is likely that the morphologic character of the lesions also must play a considerable rôle.

Beck (1905) appears to have been the first to test the effect of radium on trachoma. He treated three patients; in two of these cases the condition was described as

[91] The Ghilarducci method involves the use of certain metals of high atomic weight, such as silver, copper, bismuth or mercury (double citrate of copper and ammonia, for instance) in the conjunctival sac, to act as secondary radiators.

cured and in one case as improved. Almost at the same time Cohn (1905 and 1906), Falta (1905), Horniker and Romanin (1905), and Zelenkovsky (1905), testified that radium caused the lesions of trachoma to retrogress rapidly. In the cases mentioned by Cohn the diagnosis was not absolutely clear, and Cohn admitted Uhthoff's contention that they were examples of follicular conjunctivitis rather than of trachoma. Moreover, many of these early records were not specific with reference to permanency of cure or duration of improvement. Birch-Hirschfeld (1905) reported having treated ten cases with 10 mg. of radium for from three to twenty minutes; rapid atrophy of the follicles ensued, and this lasted several weeks in one case, but in the nine others the disease recurred. The retrogression of the follicles was ascribed to destruction of the lymphocytes which form a large part of the granulomatous lesions. Birch-Hirschfeld concluded that radium has no advantage over other methods of treatment; Esdra (1906) and Fortunati and Esdra (1908) came to the same conclusion. Flemming (1913) treated sixteen patients with radium; two were cured permanently; four derived temporary improvement; the ten others were either not benefited or it was impossible to be certain if radium was responsible for the slight amelioration in the condition. Although these reports do not give sufficient information for analysis, the impression is gathered that failure to obtain more substantial results may have been due to inadequate treatment. This impression is strengthened by reviewing the communications of Zelenkovsky (1906), Jacoby (1906), Kardo-Sisoyeff (1906), Dinger (1906), Neuschüler and Steiner (1906), Thiebault (1906), Norton (1907), Zelenkovsky (1908), Müller and Högler (1922), Sallmann (1923), Wassing (1923), Lane (1924), and others, by whom many cases were reported in which the patients were permanently cured or temporarily improved. Prokopenko (1910), for instance, described seven cases of trachoma, in six of which the disease disappeared permanently after treatment with 5 mg. of radium bromide; the seventh patient improved greatly, but the long duration of the disease prevented its complete regression.

Terrien (1919) admitted the influence of radium on trachoma, but stated that the lesions were prone to recur. May (1912) and Derby (1924), on the contrary, were unable to concede radium any value. May employed celluloid plates coated with radium bromide (of a radioactivity of 25,000) and inserted beneath the lids of the right eye for ten minutes three times a week for three months; the left eye was treated with copper sulphate. May's failure can probably be accounted for by the weakness of the radioactive source employed. Derby had no personal experience.

The most common method of treating trachoma with radium has been to evert the lids and apply the radium directly to the conjunctiva in the form of a plaque or other applicator corresponding to a plaque. This method, which was undoubtedly the result of the small quantity of radioactive substance generally available, probably explains the common difficulty of causing the lesions to disappear from the region of the fornix and may account for many failures. Müller and Högler demonstrated that as good or better results can be obtained by irradiating the conjunctiva through the uneverted lids. There is no good reason why treatment with a sufficient quantity of moderately filtered radium should not yield results as favorable as those which follow roentgen irradiation. It is indisputable, however, that, owing to the proximity of the radium to the eye, in comparison with the relatively

great distance at which roentgen irradiation is given, the latter makes for greater uniformity of irradiation and is less inconvenient to the patient.

Exposure to roentgen or radium rays causes the granules to diminish rapidly in size and number and to disappear. This is accompanied by early relief from pain and improvement in the other symptoms. The effect of irradiation is often perceptible within a week or two and sometimes within a few days. With the exception of the report of Harman (1905), all the foregoing reports concur in this respect. Even those who, like Terrien, were disappointed by the tendency of the disease to recur, described the prompt and marked influence of the rays on the lesions. Sabbadini (1926) whose communications are probably the best on the subject, clearly showed that irradiation causes the lymphoid elements and granulomatous papillae to disappear and to be replaced by young connective tissue, and the epithelium to regenerate. Such rapid and pronounced action of roentgen rays on the lesions which characterize trachoma can readily be accounted for by the great radiosensitiveness of lymphocytes. This explanation, advanced by Zelenkovski (1905) in connection with radium, is undoubtedly sound; the microscopic studies of Sabbadini establish this clearly. Additional evidence is to be found in nearly all the foregoing reports in the small doses of roentgen rays required to produce the effects described. Cochard, for example, gave doses of from one-fifth to one-fourth of a Holzknecht unit from six to nine times in the space of two or three months. It would be difficult to explain such a sequence of events on any other basis. Sabbadini (1924) observed, in three cases of bilateral cicatricial trachoma and marked pannus, that roentgen-ray treatment directed to one eye was followed by improvement in both the irradiated and unirradiated eye. This observation has not been duplicated by anyone else, although many others who have employed radiation successfully in trachoma also treated only one eye and left the other eye unexposed for comparison.

Tuberculous Conjunctivitis. Tuberculosis of the conjunctiva seems distinctly amenable to radiotherapy. The first example of such effect appears to have been recorded by Bettremieux (1903). The patient was a young girl with tuberculosis of the conjunctiva and cornea, and marked improvement followed exposure to roentgen rays. Stephenson (1903) reported the case of a child aged four years, in which the conjunctival tuberculosis was cured by thirteen sessions of roentgen-ray treatment in seven weeks. Tuberculosis of the cervical lymph nodes developed later, and they were removed surgically. Von Hippel (1918) cited the case of a boy aged fourteen with tuberculous conjunctivitis, in which twelve exposures to roentgen rays in three months brought about a complete cure. Jendralski (1921) reported eight cases of tuberculous conjunctivitis and iritis, in some of which the inflammatory process was advanced or complicated by tuberculosis in other organs. The ocular tuberculosis was cured by roentgen-ray treatment alone in two cases, improved in two others, but cure or improvement in the four other cases occurred only after treatment with tuberculin or ultraviolet rays. In some of the cases the improvement was only temporary; the disease recurred in one case and was fatal in another. Hensen and Schäfer (1924) recorded apparent cure in three additional cases of tuberculous conjunctivitis with chronic blepharitis. Mylius (1927) observed rapid regression of the tuberculous process in the conjunctiva of two patients treated with radium or mesothorium, but he did not report on the subsequent course of the disease.

Lupus of the conjunctiva also appears susceptible to irradiation, if one may judge

by the testimony of AUBINEAU and CHUITON (1908), who cited the case of a girl aged fifteen, with involvement of the conjunctiva and cornea, cured by means of roentgen rays. PISSARELLO (1915), PUSEY (1918) and HORVATH (1927) also furnished evidence that radium has much the same effect as roentgen rays on conjunctival tuberculosis.

Vernal Conjunctivitis. Radiotherapy is now regarded by many ophthalmologists as the best available method of dealing with so-called vernal conjunctivitis, and yet the number of cases reported in the literature is much smaller than the number of cases of trachoma. ALLPORT (1903) reported the first instance of a patient cured by means of roentgen rays, and the patient was well one year later. Pusey recorded another case during the same year. Additional cases were described later by Pardo (1904–1905), ZENTMAYER (1906), GONZALES (1920), GUARINI (1922), and others. The beneficial effect of the treatment is rapid; in many of the cases described the patients were cured permanently, but in others they were only improved.

The first to submit evidence that radium has a beneficial effect on the lesions of this disease seems to have been GUGLIANETTI (1908), who treated only one eye in each of two cases; considerable improvement in the irradiated eye was noted in both cases. Unfortunately, the subsequent course of the disease could not be watched, and Guglianetti was unable to draw conclusions. DAVIDSON and LAWSON (1908–1909) presented the first example of complete cure of the disease in a boy aged twelve, who had been treated unsuccessfully by other methods for one year. LAWSON and DAVIDSON, in 1910, recorded two more cases in which the patients were cured or improved. Since that time many other instances of cure or improvement have been described by MACKAY (1911), SCHNAUDIGEL (1912), BUTLER (1916, 1917), DE GILLEUMA (1918), Pusey (1918), SHUMWAY (1918), JANEWAY (1920), New and Benedict (1920), HORNER (1921), Broeman (1925), and others. In many, but not all, of the cases included in the foregoing reports the patients were cured permanently. It is probable that inadequate or improper treatment may account for the occasional failure to obtain complete resolution of the inflammatory process, but other, uncertain, factors also may be responsible.

The evidence that roentgen and radium rays have a beneficial effect on vernal conjunctivitis is less abundant than, but just as conclusive as, that which relates to trachoma. If this evidence has been more generally accepted, it is probably because some of the contributors have been better known. The mechanism involved in the improvement or cure of the condition has never been elucidated, but from the character of the disease it seems likely that the chief factor is the action of the rays on the leucocytes infiltrating the conjunctiva. It is curious that so many more patients have been treated with radium than with roentgen rays. The reason appears to be that a large proportion have been treated by ophthalmologists and not by radiologists. Certainly, economy of time, inconvenience and cost to the patient, and absence of physical discomfort favor roentgen in preference to radium treatment, especially since the results are essentially the same. Eversion of the lids during the treatment and heavy doses are unnecessary and even undesirable.

Other Diseases of the Conjunctiva. The cure of pterygium after treatment with radium was obtained by Broeman (1925) in one case. WITHERS (1924) expressed a favorable opinion on the influence of radium on pterygium, but the basis for this

opinion is uncertain. Broeman (1925) also mentioned a patient with ocular pemphigus in which the disease disappeared after radium irradiation.

Simple Keratitis. Roentgen rays apparently have a certain influence on inflammatory processes affecting the cornea. The literature contains many references to such action; some of these reports deserve little confidence, but others can hardly be questioned. Coleman (1907) mentioned a case of relapsing keratitis in which substantial benefit was derived from roentgen-ray treatment. Sgrosso (1922) called attention to the great benefit derived from irradiation by a woman aged twenty-two with parenchymatous keratitis of the left eye and by a girl aged sixteen suffering from keratitis and iritis of the right eye. The inflammation and symptoms subsided rapidly after a total dose of 4 Holzknecht units divided into six sessions at intervals of six to eight days. Lawson and Davidson (1910) reported seven cases of acute keratitis, in five of which cure or much improvement was secured by exposure to radium.

Corneal Opacity. The first mention of the beneficial effect of irradiation on corneal opacity seems to have been made by F. H. and C. H. Williams (1904); the corneal opacity was associated with uveitis, and definite improvement followed treatment with radium. Other cases were recorded by Linnell (1909) and Fellows (1910) as the result of roentgen-ray treatment, and by Lauber (1921) and Lane (1924) after exposure to radium.

Ulcerative Keratitis. Several instances of cure or marked benefit from irradiation in ulcers of the cornea have been described, and some of these instances are fairly convincing. Coover (1909) reported the cure of a man aged thirty-seven with corneal ulcer and the improvement of three other patients from roentgen-ray treatment. Flemming (1913) cited seven cases of ulcer of the cornea. Three patients were cured by radium or mesothorium; one was greatly benefited, and radiotherapy had no effect on the three others. A brief mention of another case, in which apparent improvement followed roentgenization, was made by Hunter (1920). Examples of the beneficial influence of radium were recorded by Lawrence (1909) and Lawson and Davidson (1910), and Cuperus (1917) noted great improvement following treatment with mesothorium in a case of corneal ulceration in both eyes. The success of Lawson and Davidson (1910), who were able to cure sixteen of seventeen patients with ulcers of the cornea by treatment with radium, is of decided interest. Lane (1924) also reported six cases of corneal ulceration in which radium brought about rapid improvement; in three cases the ulcers healed without any visible scar.

Interstitial Keratitis. This form of keratitis, which is so generally regarded as specific, appears to be definitely amenable to radiotherapy. Such, at least, is the conclusion to be drawn from the contributions of Japiot and Bussy (1921, 1923), Guarini (1922), Bywater and Plummer (1923), de Courcy and Mather (1924), and De la Vega (1924), who have recorded several instances of cure or pronounced amelioration. The action of radium and mesothorium on this disease is apparently the same as that of roentgen rays, if we may judge by the reports of Norton (1905), Koster (1913), and Lane (1924). Flemming (1913), on the contrary, had little if any success in ten cases in which radium treatment was used. Janeway (1920) also failed to observe any improvement of the only patient with interstitial keratitis treated by him. Japiot and Bussy reported the cure of marked interstitial keratitis in two children with hereditary syphilis, and stated that the best results were ob-

tained in cases of children and of patients with marked inflammatory reaction. They added that a definite analgesia was the first perceptible effect of irradiation, and that only small doses are necessary. All of which indicates that the results of exposure to roentgen or radium rays are due chiefly to destruction of the leucocytes (lymphocytes) infiltrating the affected ocular tissues.

Tuberculous Keratitis. The animal experiments of Takahasi would lead one to expect a definite influence of roentgen and radium rays on tuberculous processes in the eye, and this expectation is at least partly fulfilled. Bettremieux (1903) was the first to furnish evidence of the influence of roentgen rays on ocular tuberculosis in the case of a young girl with tuberculous keratitis and conjunctivitis, who improved greatly following roentgen irradiation. Mylius (1927) also presented evidence of the therapeutic influence of roentgen rays in five cases of tuberculosis of the cornea. The tubercles disappeared completely from the cornea of four of these patients, and they remained free from recurrence for an unspecified period. Koster and Cath (1911) treated with radium four patients with parenchymatous tuberculosis of the cornea, and reported marked improvement of three. Koster (1913) wrote that mesothorium is most effective in tuberculosis of the cornea, but did not give details. Cuperus (1914) reported the cure, with improvement in vision, of a patient with diffuse scrofulous keratitis, and in 1917 he described three additional cases in which substantial benefit had been derived from mesothorium. Another instance of marked improvement following radium treatment was recorded by Lane (1924). In some of these cases the lesions were not confined to the cornea, but also involved the iris. Wassing (1924) also mentioned a woman aged forty-nine, in whom radium treatment induced the disappearance of tuberculous nodules from the iris.

Scleritis and Episcleritis. Roentgen and radium rays sometimes exert a favorable influence on these conditions. Pardo (1904–1905), and Coleman (1907) each reported one case of episcleritis, in which the patient was cured, and Pardo another case in which scleritis improved, by roentgen rays. Thiébault (1906) mentioned three patients with episcleritis, one of whom was cured, and two temporarily improved, by treatment with radium. Koster (1913) stated that tuberculosis of the sclera responded well to mesothorium, but this assertion was not supported by any case report. Wassing (1924) described a patient with tuberculous scleritis, keratitis and iridocyclitis, whose lesions completely disappeared following treatment.

Simple Iritis. Simple inflammation of the iris and ciliary body often reacts favorably to roentgen or radium irradiation. Instances of the beneficial action of the rays have been reported by Coover (1909), Sgrosso (1922), Handman (1924), and others. Coover mentioned a man aged forty-seven, with serous iritis, in whom all the inflammatory manifestations disappeared after nine series of exposures to so-called roentgen-ray flashes. This method of treatment is considered elsewhere (page 61). Coover also cited the case of a woman aged sixty-five, with iritis, whose vision had been lost after an operation for cataract. Iridectomy performed several years later was followed by cyclitis, and subsequent iridotomy was unsuccessful; her condition was reported to have improved distinctly after roentgen-ray treatment by the so-called "flash" method, but the data furnished are incomplete. One of the patients mentioned by Sgrosso was a girl aged sixteen with iritis and keratitis, and the other a woman aged forty with bilateral iridochoroiditis; the ocular condition of both improved greatly after the eyes had been exposed to 4 Holzknecht units of roentgen

rays generated at 145 kilovolts, filtered through 4 mm. of aluminium, and divided into six sessions at intervals of from six to eight days. Pordes (1926–1927) and Horvath (1927) also produced evidence of the beneficial influence of radiation on iritis. Horvath treated sixty-two patients and stated that in acute cases a single irradiation was sufficient to stop the inflammatory process which did not recur.

Darier (1902–1903) obtained rapid and marked relief from pain in a case of acute blennorrhagic iritis by means of radium. Similar relief from pain was noted soon after radium treatment in three cases of iridocyclitis. Rapid improvement of iritis also occurred in two cases following treatment with radium by Lane (1924).

Tuberculous Iritis. Tuberculosis of the iris and ciliary body also appears susceptible to irradiation. Rollet and Bussy (1920) described a patient with nodular tuberculosis of the iris in which roentgen-ray treatment was followed by complete disappearance of the disease. Jendralski (1921) described eight cases with tuberculous invasion of the iris, in most of which improvement followed exposure to roentgen rays, in spite of the fact that the disease was sometimes quite extensive. Two were still well three and five years, respectively, after irradiation; the condition of the other two patients improved, whereas the remainder were cured or improved only after exposure to roentgen rays was supplemented by tuberculin or ultraviolet rays. There was recurrence in one case, and one patient died. Birch-Hirschfeld (1923) and Stock (1925) also testified to the value of roentgen-ray treatment in tuberculous iritis and iridocyclitis, without giving any personal evidence to substantiate their claim. Scheerer (1925) treated with roentgen rays thirty-six patients with tuberculosis of the iris and ciliary body, with more or less subsidence of the disease in most instances. Complete disappearance of tubercles did not occur in cases in which one or two treatments were given, but some of the patients exposed to roentgen rays three or more times at intervals of one or two months were cured and remained well; the condition of others proved refractory. Stock (1926), working with Scheerer, also testified to the favorable effect of roentgen-ray treatment on tuberculous iritis. His report was based on fifty such cases, including the thirty-six previously recorded by Scheerer (1925). From this experience Stock concluded that tuberculous iritis gives the best results, that scleritis and sclerosing keratitis also heal with surprising rapidity, but that cyclitis and choroiditis do not respond so well. More conservative was the contribution of Wetterstrand (1926), who, nevertheless, found roentgen irradiation of decided value in most of seventeen cases. The experience of Mylius (1927) was much the same. He treated twelve patients with iridocyclic tuberculosis, but several were not completely cured, either because they were insufficiently treated or because the disease proved refractory. Martenstein and Richter (1927) have given a most interesting and favorable report of their experience with roentgen-ray treatment in forty cases of tuberculous iritis. The majority of the patients derived great benefit and many of them were completely cured. Martenstein and Richter found that the best results were obtained in the early, proliferative phase of the lesions, with doses approximating 25 per cent of an erythema skin dose of roentgen rays generated at 150 peak kilovolts. They added that, after a transient phase of reaction lasting about twenty-four hours, the eye became paler, the formation of exudate ceased, the precipitates disappeared, and the tubercles retrogressed. Moreover, recurrence did not take place in any of the

twenty-nine patients dismissed as cured, although some were observed as long as eight years.

Instances of the favorable influence of mesothorium were reported by Koster (1913) and Cuperus (1914 and 1917). Cuperus (1914) mentioned a patient with bilateral tuberculous iritis in whom the tubercles disappeared, the iritis subsided, and vision increased from 5/20 and 5/30, respectively, to 5/10 in both eyes as the result of treatment with mesothorium. Wassing (1924) also recorded three cases. One patient, a woman, aged thirty-five, had tuberculous iritis which had not improved under treatment with tuberculin; exposure to 600 milligram-hours of radium caused the lesions to retrogress and the corneal opacity to diminish. The second patient, a woman, aged thirty-nine, with tuberculous iridocyclitis, recovered normal vision after exposure to 870 milligram-hours of radium, and the tuberculous process improved greatly. The third patient, a woman, aged forty-nine, with tuberculous iridocyclitis associated with scleritis and keratitis, was exposed to 830 milligram-hours of radium, and the tuberculosis disappeared.

Cataract. Norton (1905) attempted to influence an immature cataract by radium treatment, but the attempt proved unsuccessful. Norton's failure did not encourage others to test the possible value of radiotherapy in cataract until 1919, when Cohen and Levin wrote that they had treated twenty-four patients with some success. The cataracts were senile in twenty of these cases, and in four the condition was complicated by retinitis, iridocyclitis, and chronic glaucoma. Three patients were treated for one year, three for eleven months, two for ten months, two for nine months, six for eight months, two for seven months, three for four months, and three for three months. Diminution in the opacity of the lens and improvement in vision were noted in twelve cases. The lenticular opacity disappeared in one case, without any increase in visual acuity. In five cases the opacity diminished but vision remained stationary. Vision improved in three cases, but the opacity of the lens remained unchanged. Change in the condition in three other cases was not observed. Franklin and Cordes (1920) reported having treated thirty-one patients with cataract with a plaque containing 9.95 mg. of radium bromide; in 84.3 per cent there was improvement of vision. Lane (1924) also noted improvement of three patients with cataract after radium treatment. Koster (1913), on the contrary, did not observe any effect on cataract from irradiation by mesothorium.

Such meager evidence can hardly be said to establish the value of radiotherapy for cataract. Certainly, the case in favor of radiotherapy does not appear strong, and what is known about the influence of roentgen and radium rays on the crystalline lens does not furnish a substantial or even plausible basis on which might rest the therapeutic application of radiation to cataract. At least, further and more conclusive data must be presented before professional skepticism is overcome.

Diseases of the Choroid. Darier (1902–1903) noted rapid relief from pain following radium treatment of a patient suffering from choroiditis and periorbital neuralgia of long standing. Fellows (1910) mentioned a patient with disseminate choroiditis, whose vision improved greatly after roentgen-ray "flash" treatment. Koster (1913) stated that choroiditis, especially when due to tuberculosis, was influenced favorably by mesothorium, but did not furnish corroborative evidence. Herrnheiser and Braun (1928) described three cases of choroidal tuberculosis completely cured by exposing the eye to 70 R (1/6 erythema skin dose) of roentgen rays generated at

120 peak kilovolts and filtered through 4 mm. of aluminium several times at weekly intervals. The effect of the treatment was perceptible first in the nodules, which diminished in size and disappeared in a short time; the absorption of the exudate required more time. In 1928 they reported nine additional cases, in which the disease had apparently been made to subside or to disappear by roentgen irradiation. They observed rapid disappearance of fresh nodules and somewhat slower absorption of the exudative products. Improvement in vision paralleled the objective recovery.

Radiotherapy in Traumatic Injuries of the Eye. The inflammatory reaction associated with certain traumatic injuries of the eye also seems to be influenced by roentgen and radium rays, at least in certain cases. AXENFELD (1917) made favorable mention of the value of radium in cystic iritis following trauma, and related one instance in which radium had inhibited the epithelial proliferation. VIGANO (1920) found irradiation useful in favoring the resolution of adherent scars, and the absorption of hemorrhagic effusions, exudates, and inflammatory infiltrates; he reported six cases of traumatic injury to the eye from war explosives, and one with separation of the retina, in which distinct improvement followed roentgen-ray treatment. Jendralski (1922) recorded the case of a patient who had sustained an injury of the cornea from a hand grenade. Cysts formed in the corneal scar. Four days after a strong dose of roentgen rays (20 X units) glaucoma threatened, and the eye was operated on; the cyst was incised, the vitreous prolapsed, and the wound closed. The symptoms disappeared almost completely. The result was attributed to irradiation, but this is uncertain. Handman (1924) described the case of a man aged forty-two who had received a fragment of iron in the right eye; the iris was cut, the lens became cloudy, and vision diminished. Removal of the fragment by means of a magnet was followed by excessive proliferation of the corneal epithelium, and two cysts formed in the nasal end of the scar. Constant irritation of the eye led, one year later, to rupture of the cysts by forceps, but a new cyst developed. Four twenty-minute exposures to roentgen rays caused the cyst to diminish gradually and then to disappear.

Diseases of the Retina. HESSBERG (1926) reported having treated with some success five patients with retinal hemorrhage from trauma in one instance, from arteriosclerosis in two instances, and from tuberculosis and syphilis, respectively, in two other instances. Only one eye was exposed to irradiation, and the blood is stated to have been absorbed more rapidly and vision to have improved more in the irradiated than in the unirradiated eye.

Darier (1902–1903) noted rapid improvement after radium treatment of a man with hemorrhage into the vitreous, but Norton (1905) found radium ineffective for a patient with retinal hemorrhage. Koster (1913) wrote that in three cases of chorioretinitis treated with radium or mesothorium the condition had been influenced favorably, but that little if any effect had been noted in ten cases of retinitis pigmentosa.

Glaucoma. It is not easy to understand how irradiation could have any great or lasting effect on glaucoma. Yet Linnell (1909) reported improvement of patients with glaucoma following roentgen-ray treatment, and Guarini (1922) claimed that the disease is favorably influenced by exposure to the rays. CORBETT (1924) described three patients with glaucoma. One, a man aged sixty-two, with glaucoma and blindness of the right eye, was said to have been greatly benefited by treatment with

radium, and two other patients were slightly improved for a time. Hensen and Schäfer (1924) reported the cure of one patient with glaucoma and hemorrhage, and the improvement of five other patients with simple glaucoma. Lloyd (1927) cited the instance of a woman aged seventy, who had undergone a successful operation on the right eye for cataract and who also had a mature cataract in the left eye. Hemorrhagic glaucoma developed later, and, on the patient's refusal to allow this eye to be operated on, roentgen-ray treatment was resorted to. The pain soon disappeared, and three irradiations kept the symptoms in abeyance for two years. Similar relief from pain in glaucoma was noted in two cases by Deutsch (1928). The relief from pain may perhaps have been due to the action of the rays on the inflammatory process which may have been responsible for the glaucoma in these cases, but the evidence is not sufficient to provide a satisfactory explanation, either of the effect of irradiation on the glaucoma itself or on the pain associated with it. In glaucoma due to, or associated with, intra-ocular hemorrhage, early irradiation may cause the extravasated blood to be rapidly absorbed, and may thus influence the glaucomatous process. Evidence of such absorption of blood will be presented when the effect of radiotherapy on hematoma of the ear is discussed.

The foregoing clinical evidence indicates that roentgen rays and radium have a definite influence on certain diseases of the eye. In trachoma the rays have been shown to act chiefly on the lymphocytic infiltration. The same mechanism may explain the effect of irradiation on other varieties of ocular inflammation, but no specific statement can be made until more thorough investigations have been carried out. Nevertheless, the evidence available points in this direction. Even if allowance be made for errors in diagnosis and many cases excluded for insufficient data or incomplete examination, there remain a sufficient number of authentic and carefully studied cases to command professional attention.

Roentgen-ray Flashes, or So-called Intermittent Roentgen Treatment of Ocular Disease. In 1909 Linnell reported having treated two patients with detachment of the retina, three with glaucoma, twelve with cataract, eight with amblyopia, three with corneal opacity, and four with optic atrophy by means of roentgen-ray flashes, and claimed that all but three had derived benefit. It is difficult to understand how intermittent flashes of roentgen rays could be more effective than continuous irradiation. Moreover, the evidence submitted was insufficient to explain how intermittent irradiation could influence a condition such as amblyopia. Nevertheless, the notion of roentgen-ray flashes was taken up by Coover (1909), Sternberg (1910), Fellows (1910), and Cook (1910), who published eulogious accounts of the remarkable influence of the flash treatment for optic atrophy and other degenerative diseases of the eye. It was even advanced that roentgen-ray flashes reduced blood pressure. It must not be inferred that such intermittent irradiation could have no therapeutic effect, but since any therapeutic efficacy it may have possessed must have been due to the rays, the flash treatment could be only a longer method of producing the same results. It remained for Loring (1910) and Wells (1910) to give this bête noire the coup de grâce.

Injury to the Eye from Excessive Irradiation. Instances of ocular injury from excessive exposure to radiation have been recorded from time to time, but the number of such instances is surprisingly small considering the frequency with which the eye has been irradiated in connection with the treatment of various benign and malig-

nant conditions. This in itself constitutes corroborative circumstantial evidence of the comparative tolerance of the eye. The wholesome respect of the profession for this highly prized organ has prevented many patients with ocular diseases amenable to roentgen-ray or radium treatment from receiving such treatment, and this in turn has undoubtedly acted to prevent many injuries which might otherwise have occurred. Another significant deterring factor was the reports of Birch-Hirschfeld, who has been the most important single contributor to the literature of this subject. The partly unwarranted conclusions which Birch-Hirschfeld drew from his experimental studies and clinical observations made such a profound impression that many ophthalmologists and radiologists have never quite recovered their assurance and still hesitate to irradiate the eye for fear of injury.

In considering the possible injurious effect of excessive irradiation it is essential to analyze separately injuries resulting from single or repeated exposures, such as are used in treating patients, and injuries arising from the frequent repetition of small doses over a long period of time, such as injuries received by radiologists, whose eyes are exposed to the rays daily for months or years. The former represent acute radiodermatitis, at least at the outset, and the latter are the clinical expression of a reaction of the tissues to long-continued or oft-repeated irritation. As an example of the first variety, KING is cited by SHERER (1901) as having recorded a case in which epilation of the cilia and brows, edema and desquamation of the lids, and conjunctivitis followed roentgen-ray treatment. Most of the instances of radiation injury to the eye have been incidental to the treatment of ocular or orbital tumors with roentgen or radium rays and have been due to over-exposure. They constitute glaring exceptions to the large number of similar tumors which have been treated with more or less success and without the slightest untoward effect on the unaffected part of the eye. Indeed, some of the cases reported as examples of radiation injury were really due to other causes. Thus, CAUTLEY and HARMAN (1916) cited the case of a boy aged eight years and nine months, who, one week after receiving roentgen-ray treatment for ringworm, had frontal pain, and examination disclosed marked neuroretinitis, with striation and swelling of the optic disks, incoördination of the right hand, and jerking and twisting of the limb. The vision remained normal and there was no paralysis. The hair fell from the head, but grew again later, and the other symptoms subsided. Although the pain in the head had begun before the exposure to roentgen rays, the coincident optic neuritis was reported as possibly due to irradiation, a wholly unwarranted deduction.

Birch-Hirschfeld (1904) reported four cases; the first patient, a man aged sixty-four years, had an ulcerating epithelioma on the outer border of the left orbit; the second patient, a man aged sixty-three years, also had an ulcerated epithelioma at the outer canthus of the left eye. In both cases, the lesion was exposed to roentgen rays, and after a latent period of fourteen and eight days, respectively, complete or partial loss of eyelashes, conjunctivitis, and keratitis occurred, but subsided gradually. All the circumstances described in connection with these two patients point to irradiation as the cause of the inflammatory reaction. Not so in the third patient, a woman aged fifty-eight years with an epithelioma in the region of the inner canthus of the left eye and corresponding lacrimal sac, extending to the nasolabial fold. After several fruitless operations and final exenteration of the orbit, "during which the neoplasm ruptured through the naso-orbital wall," the region was cauterized

and shortly afterward irradiated three times in three days.[92] Ten additional exposures were made later, the right eye being always protected with stanniol and lead plates.[93] The malignant process recurred and was again irradiated. Conjunctivitis and keratitis developed later in the unirradiated and carefully shielded right eye, and Birch-Hirschfeld attributed this to the action of the rays. The circumstances make it difficult to accept such an interpretation, and the inflammation of the conjunctiva and cornea of the right eye probably originated by direct extension from the infected neoplasm invading the tissues around the root of the nose. The fourth patient, a man aged fifty-nine years, had a large epithelioma in the region of the right temple, and the growth, which was fixed to the underlying bone, had destroyed the outer third of the right upper lid and interfered with the movements of the right eye. Several exposures to roentgen rays and several probe dissections accomplished little, and the extension of the tumor continued. The region occupied by the neoplasm was then subjected to massive irradiation of 24 Holzknecht units in forty-five minutes. Conjunctivitis and keratitis occurred after each exposure to the rays and were still more severe after the last irradiation. Extension of the tumor to the conjunctiva and cornea and blindness led to enucleation. Microscopic examination showed increase in connective tissue and marked epithelial hyperplasia of the cornea with scattered nuclear and cellular disintegration, leucocytic infiltration, marked endothelial degeneration, cellular proliferation of the intima and narrowing of the lumen of the blood vessels of the iris, which was partly adherent to the posterior surface of the cornea, marked cystic degeneration of the retina, and vascular degeneration of the intima of the retinal vessels. Birch-Hirschfeld regarded all these changes as probably due to the direct action of roentgen rays on the various ocular elements, but this view is warranted only in part. The changes in the blood vessels of the iris and retina were probably the direct result of irradiation, but the pigment changes in the iris, and the degenerative changes in the retina were probably secondary to the inflammatory, neoplastic and vascular changes. Birch-Hirschfeld (1907 and 1908) reported additional cases, some of which provided clear evidence of radiation effect on certain ocular structures, such as the lids, conjunctiva, cornea and iris, while in others the presence of a malignant tumor beclouded the issue.

In some of the other cases related as examples of radiation injury the relation between the rays and the findings given is obscure and their authenticity can be seriously questioned. Ehnhuus (1919) mentioned a patient aged sixty-seven with an epithelioma[94] around the inner canthus of the right eye; the vision was normal and the ophthalmoscopic examination negative. With the eyeball protected with lead, the lesion was given nine exposures to from 3 to 5 Holzknecht units[95] of roentgen rays[96] in twenty days. During this period of irradiation the eye became red, the patient complained of loss of vision, photophobia, lacrimation and slight mucous secretion. Vision was 6/21. The skin and eyelashes were normal, but the bulbar conjunctiva was markedly injected; the cornea, lens, and iris were normal. Ophthalmoscopic examination disclosed blurring of the papilla, yellowish-white plaques in the retina, and diffuse changes in pigment. The conjunctival irritation subsided, the

[92] The dose was not clearly specified.
[93] Thickness not given.
[94] The epithelioma had developed and been treated in 1911 and 1912.
[95] It is not clear whether 3 to 5 Holzknecht units were given each time or whether this represented the total dose.
[96] The rays were described as hard, but the quality was not otherwise specified.

patient recovered normal vision, and the retinal plaques were more white and atrophic. Irradiation probably had nothing to do with the symptoms and other conditions; it is inconceivable how the lead-protected eyeball could have been injured and the unprotected lids remain unaffected by the rays, but much more likely that the ocular disturbance had another cause.

WILKINSON (1920) described a woman, aged forty, who had suffered for some time from erythematous lupus of the cheeks. She had received roentgen-ray treatment to the face for two and a half years: thirty-six exposures (every ten days) during the first year, and an equal number during the subsequent one and a half years. The eyes had never been protected during the exposures. Double cataract developed, for which operation was performed later with complete success. This may well be an authentic instance of radiation injury. Considering the age of the patient, it is quite possible that the lenticular degeneration may have been due to the frequent irradiation of the unshielded eyes for such a long time. A similar case was recorded by MOORE (1931). FISCHOEDER (1920) reported conjunctivitis and keratitis occurring in a patient with a tumor in the choroid who had received 300 Fürstenau units of roentgen rays ten times in ten days.

KÜMMELL (1921), in a series of cases[97] in which strong doses of roentgen rays of short wave-length had been used to treat malignant tumors of the eyelids, observed erythema, increased pigmentation, epithelial desquamation, thickening and ptosis of the lids, late telangiectasis of the conjunctiva, decrease in sensitiveness and tendency to superficial ulceration of the cornea. Pathologic alterations in the crystalline lens and retina were not found in any of the patients. Visual acuity sometimes diminished, but only in proportion to the degree of inflammatory exudate or ulceration of the cornea, and the vision improved as the exudate or ulceration subsided. A transient increase in intra-ocular tension, but without any clinical signs of glaucoma, was noted in two cases. The decrease in irritability of the cornea was sometimes so great that it could be indented deeply without eliciting a protective reflex. Kümmell regarded this as an effect of irradiation on the terminal nerve endings, but it was probably secondary to the inflammatory changes and connective tissue proliferation in the conjunctiva and cornea.

Another possible example of radiation injury to the eye was mentioned by PETER (1924). In a case of tumor of the eye, from a half to three-fourths of an erythema skin dose of roentgen rays generated at an unstated voltage was given to the cornea and conjunctiva, several times at intervals of from four to fourteen days. The tumor receded for a time, but recurred five months later, when the eye became glaucomatous, the lacrimal duct was obliterated, the conjunctiva became telangiectatic, and the eye was enucleated. It is difficult to be certain what part roentgen rays had in the development of glaucoma, because the tumor may have been the major, and perhaps the only, factor. FLÄSCHENTRÄGER (1924) reported two additional cases. One was a man aged sixty-five, with a tumor in the right eye, which radium treatment had caused to disappear for ten years. Metastasis to the jaw occurred later, and corneal pigmentation and telangiectasis around the limbus were noted. The other patient was a woman aged sixty-five, who had received roentgen-ray treatment for carcinoma of the breast. Radiodermatitis of the left side of the face occurred and this was associated with epilation of the eyelashes, inflammation and

[97] Russian war prisoners.

ulceration of the cornea, iritis, posterior synechiae, and diminution in visual acuity. Subsequently the cornea perforated, and the eye had to be enucleated. In both these cases, but especially in the latter, the influence of misdirected irradiation is indisputable. Sabbadini (1927) recorded three additional cases of epithelioma of the eyelids, in which exceptionally strong irradiation caused an inflammatory reaction of the conjunctiva, with beclouding and ulceration of the cornea in one case. Degenerative changes in the vascular endothelium also were found.

Ocular Injury to Radiologists. So far as roentgen-ray or radium injury to the eye itself from small doses repeated frequently over a long period of time is concerned, authentic cases are extremely rare, even among radiologists who have worked with roentgen rays and radium for many years. Sherer (1901) related the case of a physician, whose eyes had been exposed to roentgen rays daily for three years, in which epilation of the lids and brows, conjunctivitis, and slight retinitis had developed, all of which disappeared in one and a half months. These manifestations of excessive exposure were due, not to a cumulative effect of frequent exposure for a long time, but to a recent single over-exposure; otherwise, some of the resulting disturbances, such as the loss of eyelashes and eyebrows, must have been permanent. Bennett (1905 and 1906) reported that, ten days after testing twelve new roentgen tubes, severe inflammation of both eyes developed and continued for a month. He subsequently was obliged to wear protective glasses while examining patients and later had to give up his radiologic activities for a time. Several months afterward a twenty-minute exposure while examining a patient caused severe and prolonged conjunctivitis. This is one of the rare instances of the kind on record, probably because the conditions under which radiologists work seldom are such as to expose the eyes to doses beyond their limit of tolerance. Other instances are known to have occurred, but have not been reported. Chronic radiodermatitis of the lids, sometimes evolving into a malignant process, has been described, but this also is decidedly uncommon.

Lacrimal Gland

The close anatomic and physiologic relations of the lacrimal gland to the eye would lead one to expect that the radiosensitiveness of this gland must long ago have been submitted to experimental test, but, curiously enough, such is not the case. The only mention of the lacrimal gland in the animal experiments on the eye was made by Jacoby (1924) who, in the first animal irradiated, found the gland unaffected. However, if experiments on animals have not been conducted to determine the specific tolerance of the lacrimal gland to roentgen or radium rays, certain clinical data indicate that this acinous structure, like other secretory glands, is influenced in much the same manner by irradiation. Thus Hensen and Lorey (1922) reported having treated thirty-three patients suffering from excessive lacrimation. The eyeball was protected with lead, and irradiation was confined as closely as possible to the region of the lacrimal gland. A single exposure was given to eleven patients, and the effect of treatment was watched for some time in twenty patients. Apparently the treatment of these patients extended over a fairly long period of time, because Hensen and Lorey stated that, while the immediate results were not very good, better results were obtained subsequently as the apparatus and technique improved.

Brandt and Fraenkel (1922) described the case of a girl aged seventeen, one of

whose lacrimal sacs had been dilated for fourteen years and finally extirpated because of constant dribbling of tears. The corresponding lacrimal gland was then exposed to six erythema skin doses of roentgen rays in six sessions, within a period of three weeks, and the excessive secretion of the gland is reported to have diminished. Hensen and Schäfer (1924) announced having treated thirty-five cases of excessive lacrimal secretion with good results, but they did not regard the cure as permanent. They also mentioned having tested the effect of radiation on the lacrimal glands of animals, but did not observe any perceptible change. Lorenz (1924) is cited by Hensen and Schäfer as having succeeded in curing a patient with epiphora by treatment with roentgen rays.

Obviously, such evidence is far from conclusive; at most it indicates that irradiation depresses the secretory function of the gland in some measure, but we are still in the dark concerning the degree and duration of the secretory inhibition and the effect which may be expected from any specified dose of radiation.

Lacrimal Sac and Ducts. Falta (1905) mentioned four cases of trachoma with obstruction of the lacrimal duct, in which catheterization for several months had been fruitless and in which treatment by means of a probe covered with radium and left in the duct for ten minutes at a time yielded excellent results. Vigano (1913) recorded thirty cases of dacryocystitis and lacrimal fistula, in twenty-one of which lesions had recurred after having been operated on one or more times; eight lesions had not been operated on. In many instances the disease was of several years' duration. Eleven patients were completely cured, and thirteen were improved, by roentgen-ray treatment; the disease of five patients who had chosen to discontinue treatment continued unabated. Reduction in swelling and redness were the first effects noted; the secretion then diminished, the ulcers gradually healed, and those in which the resolution was complete did not recur. Very small doses of soft roentgen rays were repeated on alternate days from nine to seventy times. Hensen and Schäfer (1924) reported that four patients with tuberculous dacryocystitis were cured by roentgen-ray treatment. Cuperus (1914) described a patient with blenorrhea of the lacrimal sac, ulcer of the cornea, lagophthalmos, hypopion, and vision reduced to 3/50 who derived marked improvement following four irradiations with mesothorium. Kumer and Sallman (1924) also testified to the value of radium treatment in tuberculous dacryocystitis.

Mikulicz's Disease. The effectiveness of radiotherapy in this uncommon disease has been considered in connection with the action of roentgen rays on the salivary glands.

Conclusions

Experiments on animals on the sensitiveness of the eye to roentgen and radium rays have established that the effect of irradiation on the eye depends on the age of the animal. Exposure of the rapidly growing eye of young animals before birth or during the first or second month of life may cause retardation of development of the eye as a whole, developmental anomalies of the lids, progressive degeneration of the crystalline lens leading to cataract, and a curious anomaly of the retina characterized by plication of this structure as the result of the normal development of its different layers (except the internal granular layer) inside of an abnormally small eye. A moderate dose of roentgen or radium rays is sufficient to induce such changes, the degree of which varies with the dose and the subsequent period of observation.

The rapid development of the eye soon enables it to tolerate increasing doses with impunity, and three months after birth the eye of the cat and rabbit is no longer affected by doses below the tolerance limit of the skin. Lenticular degeneration in the mature eye of adult animals can still be produced, but only by doses several times greater than the erythema dose for the skin.

The conjunctiva and eyelids are the most susceptible of the ocular structures, but their specific sensitiveness is only slightly greater than that of the surrounding skin. An erythema dose of roentgen or radium rays may be followed, after a latent period of about two weeks, by loss of hair and lashes, increase in conjunctival secretion, actual inflammation of the conjunctiva and lids, or even simple or ulcerative keratitis. After a dose sufficient to cause only faint erythema of the skin of the eyelids the resulting epilation, conjunctivitis, and blepharitis are slight and of short duration. Permanent alopecia of the lids and severe conjunctivitis, blepharitis, and keratitis occur only after greater doses. The cornea, iris and ciliary body, and retina are, in the order named, increasingly resistant. All these structures can be injured by irradiation of sufficient intensity, but the cornea is much less sensitive than the conjunctiva, and the mature retina can tolerate with impunity doses several times beyond the limit of tolerance of the conjunctiva and eyelids. The degenerative changes in the retina described by Birch-Hirschfeld and attributed by him to irradiation were probably postmortem changes, artefacts due to fixation methods, or were secondary to the action of the rays on the conjunctiva, cornea, and iris. The blood vessels of the conjunctiva, iris, and retina also are affected by suitable doses of radiation; doses sufficient to cause conjunctivitis induce degeneration and later reparative proliferation of the vascular endothelium. After more intense irradiation these vascular alterations may be so marked as to lead to obliteration of the lumen of the vessels.

The action of radium on the eye is substantially the same as that of roentgen rays. Degenerative changes in the blood vessels appear to be a somewhat more prominent feature of exposure to radium, because the shorter distance between the radioactive source and the irradiated tissues allows the beta rays to exert their intense, short-range influence. Radioactive water injected beneath the conjunctiva has practically no effect on the eye, because it is carried away very rapidly. The only result of injecting radioactive water into the vitreous is a temporary haziness of the vitreous and cornea, and a transient increase in intraocular tension. Injection of a solution of thorium X into the anterior chamber causes iritis, and sometimes keratitis and conjunctivitis, and this is accompanied by degeneration of the endothelium and media of the iridian vessels. Injection of a solution of thorium X into the vitreous is followed by cloudiness of the vitreous, narrowing and occlusion or endothelial destruction and thrombosis of the retinal vessels, multiple hemorrhages, late degeneration of the lens, and sometimes by decoloration of the iris, hyperemia of the choroid and ciliary body, necrosis and edema of the pigment epithelium, and disappearance of the layer of rods and cones from the retina. Radium and mesothorium also retard the development of tuberculous lesions of the eye and cause the resolution of tubercles in the conjunctiva, cornea, and iris.

Roentgen and radium rays appear to have a definite resolving influence on tuberculous lesions of the eye; this effect seems greatest during the infiltrative stage

and least after caseation of the tubercles. A similar action of irradiation on infected, traumatic ulcers of the cornea has been shown by Sabbadini. The exceptional vulnerability of leucocytes probably explains this effect of the rays, but further studies will be required to establish this conclusively.

Many other ocular diseases appear to be amenable to radiotherapy, and many examples of the benefit to be derived from roentgen-ray or radium treatment have been reported. Among these may be mentioned certain inflammations of the eyelids; follicular, tuberculous, and vernal conjunctivitis, trachoma, and pterygium; simple, ulcerative, and interstitial keratitis, and corneal opacity; scleritis and episcleritis; simple and tuberculous iritis, and simple and tuberculous choroiditis. Not all cases of such diseases are improved by this method of treatment. The clinical evidence indicates that thorough treatment is especially effective in trachoma and vernal conjunctivitis; in the acute or subacute phases of these conditions roentgen rays or radium can almost be called specific. The action of the rays on all these inflammatory conditions of the eye seems to be to destroy the lymphocytes of the inflammatory infiltrate; pain is rapidly relieved and resolution often is prompt. It is even probable that the improvement is proportional to the degree of lymphocytic infiltration. Radiotherapy also has been found useful in favoring the resolution of hemorrhagic effusions, exudates, and infiltrates in traumatic injuries of the eye. The value of roentgen or radium rays in glaucoma is doubtful; the only form of the disease in which benefit might be expected from such treatment is that due to hemorrhage or to inflammatory processes accompanied by marked leucocytic infiltration.

Excessive exposure of the eye to radiation may injure the organ more or less severely. Examples of such injury have been reported, but in some of the cases cited as instances of injury by roentgen rays or radium the relationship between irradiation and the symptoms and clinical manifestations cannot be substantiated. Ocular injury from chronic irritation by small doses of roentgen rays or radium repeated frequently over a long period of time also may occur, but the number of authentic examples is small.

The effect of radiation on the lacrimal glands does not seem to have been submitted to experimental test, but clinical evidence indicates that the function of the gland is inhibited to some extent by exposure to roentgen rays or radium. This property of the rays to diminish the functional activity of the lacrimal gland has been applied with some success for patients suffering from excessive lacrimation. Certain inflammations of the lacrimal sac and duct also appear to respond in some measure to radiotherapy.

To be continued.